Dedifferentiated Liposarcoma with Abrupt Transition of Low-Grade and High-Grade Dedifferentiated Components ：A Case Report

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Case Report

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Abstract

Background: Dedifferentiated liposarcoma (DDLPS) is a unique subtype of

liposarcoma, which has obvious histological heterogeneity. In affected patients, the condition typically manifests as the dedifferentiation of high-grade histological morphology, but it may also manifest as the dedifferentiation of low-grade histological morphology. In some cases, unique histological or immunophenotypic characteristics are observed. We describe, herein, a rare case of dedifferentiated liposarcoma, in which the high-grade and low-grade dedifferentiated components coexisted with a relatively sharp transition in pathology.

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, Magnetic resonance imaging (MRI) scan showed a huge mass with typical fat components and the non-fatty nodule in the left retroperitoneal cavity. After laparotomy, histologic analysis of the specimens could find the ALT/WDLPS and DDLPS components. Fluorescence in situ hybridization (FISH) analysis suggested the presence of MDM2 gene amplification. These findings supported a diagnosis of DDLPS.

Conclusion: In our case, the high-grade and low-grade dedifferentiated components coexisted with a relatively sharp transition in pathology. We hypothesize that low-grade dedifferentiation may be a precursor to 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]. Although atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLPS) and dedifferentiated liposarcoma (DDLPS) have similar genetic characteristics, WDLPS and DDLPS represent two ends of the histologic and behavioral spectrum for a single disease entity[2, 3]. Histopathologically, DDLPS may show a markedly heterogeneous morphology. In most patients, the condition manifests as the dedifferentiation of high-grade histological morphology, similar to undifferentiated pleomorphic sarcoma or high-grade myxofibrosarcoma. In some cases, the condition may manifest as 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, or 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 few samples are available. In this manuscript, we retrospectively analyze 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. We also review 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 prior. The patient had begun to have abdominal cramps repeatedly over the preceding 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, and tumor markers (carcinoembryonic antigen and CA19-9) were within normal limits.

Radiologic Findings

Magnetic resonance imaging (MRI) examination showed an 8 cm × 13.3 cm × 20.9 cm mass in the left retroperitoneal cavity. The MRI signal intensity for most of the mass was hyperintense on T1-weighted images and T2-weighted images, with drop-out on MRI fat-suppressed sequences images. (Fig. 1a-1b) A 7.8 cm × 10.6 cm × 11.2 cm solid nodule was seen in the lesion with a heterogeneous signal. T2-weighted images show mixed-intensity signal. T1-weighted images showed iso-intensity signal, without signal dropout on MRI fat-suppressed sequenced images. The apparent diffusion coefficient (ADC) map showed irregular low-intensity signal at the edge of the nodule, with an ADC value of 0.913×10^{-3}. (Fig. 1c) On contrast-enhanced images, the non-fatty nodule showed irregular peritumoral enhancement and no enhancement in the central region. (Fig. 1d)

Surgical And Pathologic Features

During laparotomy, the well-circumscribed, lobulated mass, which was located in the left retroperitoneum and about 25 cm × 20 cm × 22 cm in size, underwent complete excision. 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 was approximately 20 cm × 16 cm × 7 cm, and the size of the grayish-yellow fatty mass was about 9 cm × 8 cm × 7 cm. A round nodule with a complete capsule was seen adjacent to the fatty mass, which was about 11 cm × 9.5 cm × 7 cm in size. A grayish-yellow necrotic area (about 8 × 6 × 5 cm) was seen in the nodule's center, surrounded by a crescent-shaped grayish-white and grayish-brown tumor. There was a clear boundary between brown tumor foci near the capsule and other gray-white or fish flesh-colored tumor foci. (Fig. 2)

Microscopically, there was a sharp transition between ALT/WDLPS and DDLPS. (Fig. 3a-b) Most DDLPS are high-grade undifferentiated pleomorphic sarcomas with extensive tumor necrosis, with low-grade areas near the capsule. Histologically, DDLPS have inflammatory myofibroblastic tumor-like (Fig. 3c) and fibromatosis-like features. (Fig. 3e) Multiple focal regions of the DDLPS may exhibit a sudden transition between high-grade and low-grade dedifferentiated components. (Fig. 3d/f) Immunohistochemical analysis was positive for P16, CDK4, and MDM2. Fluorescence in situ hybridization (FISH) analysis

suggested the presence of MDM2 gene amplification. (Fig. 4) These findings supported a diagnosis of DDLPS.

The patient recovered well and was discharged from the hospital on the 7th day after surgery. Followed-up was performed regularly, and there was no sign of local recurrence or distant metastasis during a 12 months follow-up.

Discussion

According to the World Health Organization (WHO) classification standards, the definition of DDLPS is a bone and soft tissue tumor or ALT / WDLPS that has dedifferentiated into a different degree of sarcoma at the same time or before/after the development of ALT / WDLPS[2, 8]. Dedifferentiated areas usually consist of undifferentiated pleomorphic sarcoma or spindle cell sarcoma, with high to moderate cellularity and pleomorphism. In 10% of DDLPS cases, low-grade sarcoma components resembling fibromatosis or low-grade fibromyxoid sarcoma are apparent[4, 7]. In contrast to ALT / WDLPS, which has a relatively clear histological subtype, DDL represent a morphologically heterogeneous group. In the case described above, DDLPS was characterized by the coexistence of high- and low-grade dedifferentiated components. This manifestation is rare in clinical practice. We summarize the associated pathological features and MRI findings to deepen the awareness of this rare type of DDLPS.

DDLPS presents most commonly in middle-aged and older adults and affects both genders equally. The condition is extremely rare in children and adolescents. The retroperitoneum is the site most frequently affected, followed by the limb and spermatic cord / paratesticular area. Rarely affected 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. There is therefore a high risk (about 28%) that dedifferentiation will be observed at the time of diagnosis[4, 7].

The histology of DDLPS usually includes ALT / WDLPS components that have transformed into non-fatty tumor components, and the two components are usually clearly demarcated under the microscope. The most common histological type of ALT / WDLPS in DDLPS is lipomatous and sclerotic. As seen in our case report, the retroperitoneal mass was huge and contained many WDLPS components, the dedifferentiated components were characterized by the coexistence of low-grade and high-grade dedifferentiated components, the low-grade components accounted for only 10% of the dedifferentiated tumor, and were located in the periphery of the high-grade components. The boundary between the two components was identified in sections of the specimen. Pathologically, there was a sudden transition between high-grade and low-grade dedifferentiated components of the DDPLS, the transition between the two dedifferentiated portions like an abrupt line. The conversion to low-grade DDLPS starts from the periphery in high-grade DDLPS. We speculated that low-grade dedifferentiation may be a precursor to high-grade dedifferentiation, this manifestation has also been reported in other case report[9]. In the central region of a tumor with high-grade differentiation, large areas of ischemic necrosis appeared, due

to poor tissue differentiation and rapid growth. In this case, the low-grade dedifferentiated tissues exhibited fibromatosis-like and inflammatory myofibroblastoid-like features.

In addition, in the differential diagnosis of fatty tumors other than ALT / WDLPS, immunohistochemical staining that is positive for 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. 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 FISH to detect the amplification of the MDM2 gene is highly specific and sensitive for the diagnosis of DDLPS, especially when diagnosed with small biopsy specimens. The use of FISH is even more specific and sensitive in small biopsy specimens without typical WDLPS components or low-level dedifferentiation and in rare types of DDLPS[7, 10]. Amplification of the MDM2 gene is generally considered as the gold standard for the diagnosis of ALT / WDLPS and DDLPS.

The diagnosis of DDLPS requires the existence of two components in the tumor: lipogenic WDLPS and cellular nonlipogenic sarcoma. MRI can easily be used to identify fat-derived components in tumors through the use of fat-suppressed T2 images or short tau inversion recovery (STIR) imaging[11]. These approaches allow for the identification of WDLPS components in DDLPS, which is more helpful for diagnosis; however, in some cases, the WDLPS composition may go unnoticed. Because DDLPS is the conversion of WDLPS components to non-fat-derived tumor components, DDLPS lesions may lack signs of lipid characteristics on MRI. In addition, the ADC value of DDLPS lesions is low, indicating poor differentiation of tumor tissue. Dynamic contrast-enhancement of MRI can also be used to delineate the blood supply to the active area of the lesion, as well as the extent of necrosis or mucinous cystic changes in the lesion. Despite the existence of a clear transition between high- and low-grade differentiation components of DDLPS in the case described above, MRI failed to distinguish them.

In summary, for the diagnosis of liposarcoma, whether based on MRI or pathology, we should pay attention to typical fat components. MRI has some limitations when used for the preoperative diagnosis of liposarcoma in samples lacking fatty components or for the diagnosis of liposarcoma. The differential diagnosis for 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 avoid the misdiagnosis of DDLPS, it is sometimes necessary to perform immunohistochemistry (such as MDM2 gene amplification). The transition between high- and low-grade differentiation components of DDLPS characterized in this case report is an important aspect of rare pathological manifestations of DDLPS.

Abbreviations

ALT
Atypical lipomatous tumor; WDLPS:Well differentiated liposarcoma; DDPLS

Dedifferentiated liposarcoma; MRI
Magnetic resonance imaging; WHO:World health organization; ADC:Apparent diffusion coefficient; FISH:Fluorescence in situ hybridization; STIR:Short tau inversion recovery; DWI:Diffusion-weighted imaging

Declarations

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Conflicting interest

The authors disclosed no conflicts.

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Authors contribution

Dr. Yang wen and Dr. Ming Zhao 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 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

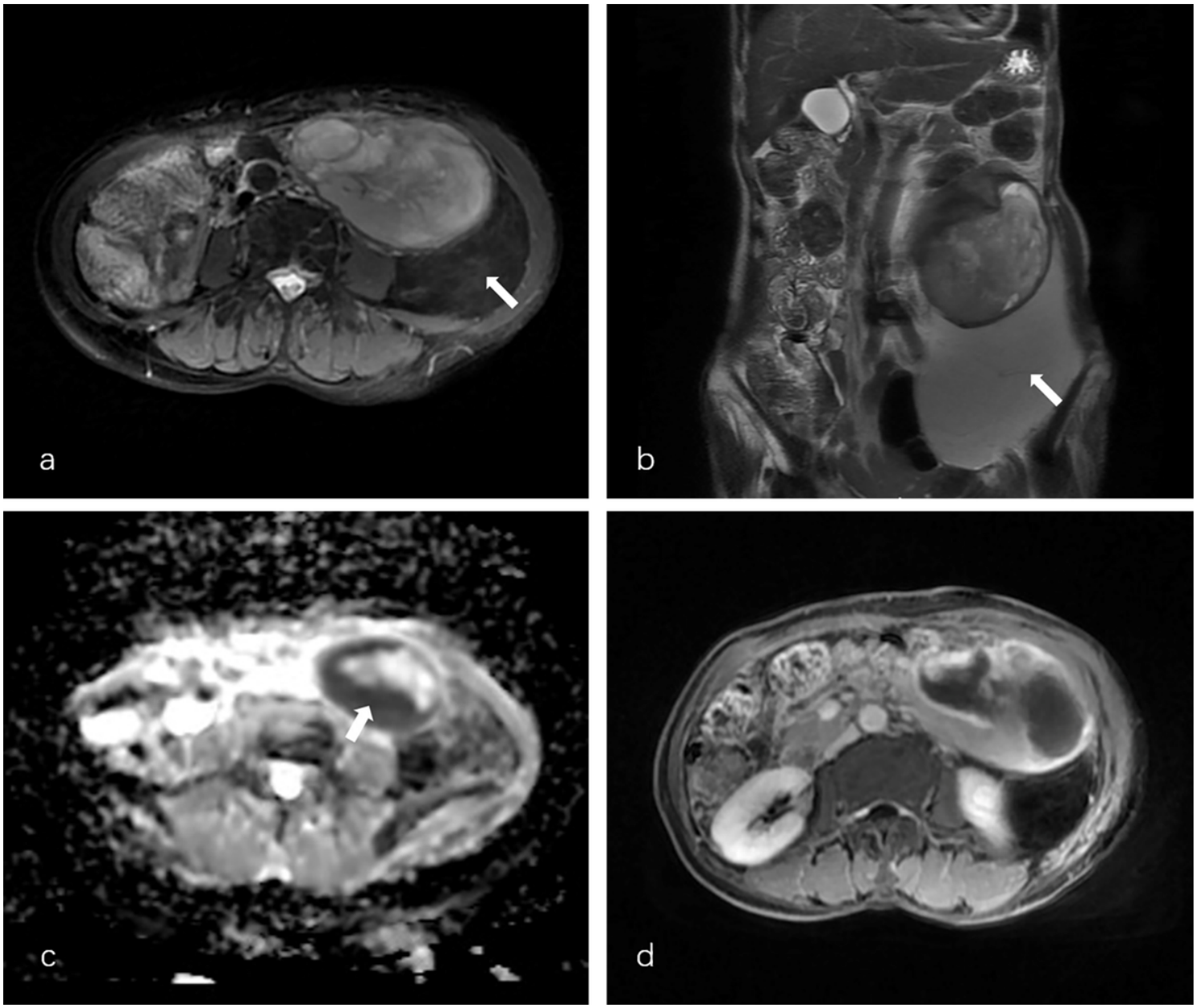

Figure 1

MRI images of DDLPS (a-b) Axial fat-saturated T2-weighted image (a) and coronal T2-weighted image (b) show a relatively well-defined pure fatty mass (white arrows), surrounding a non-fatty solid 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.

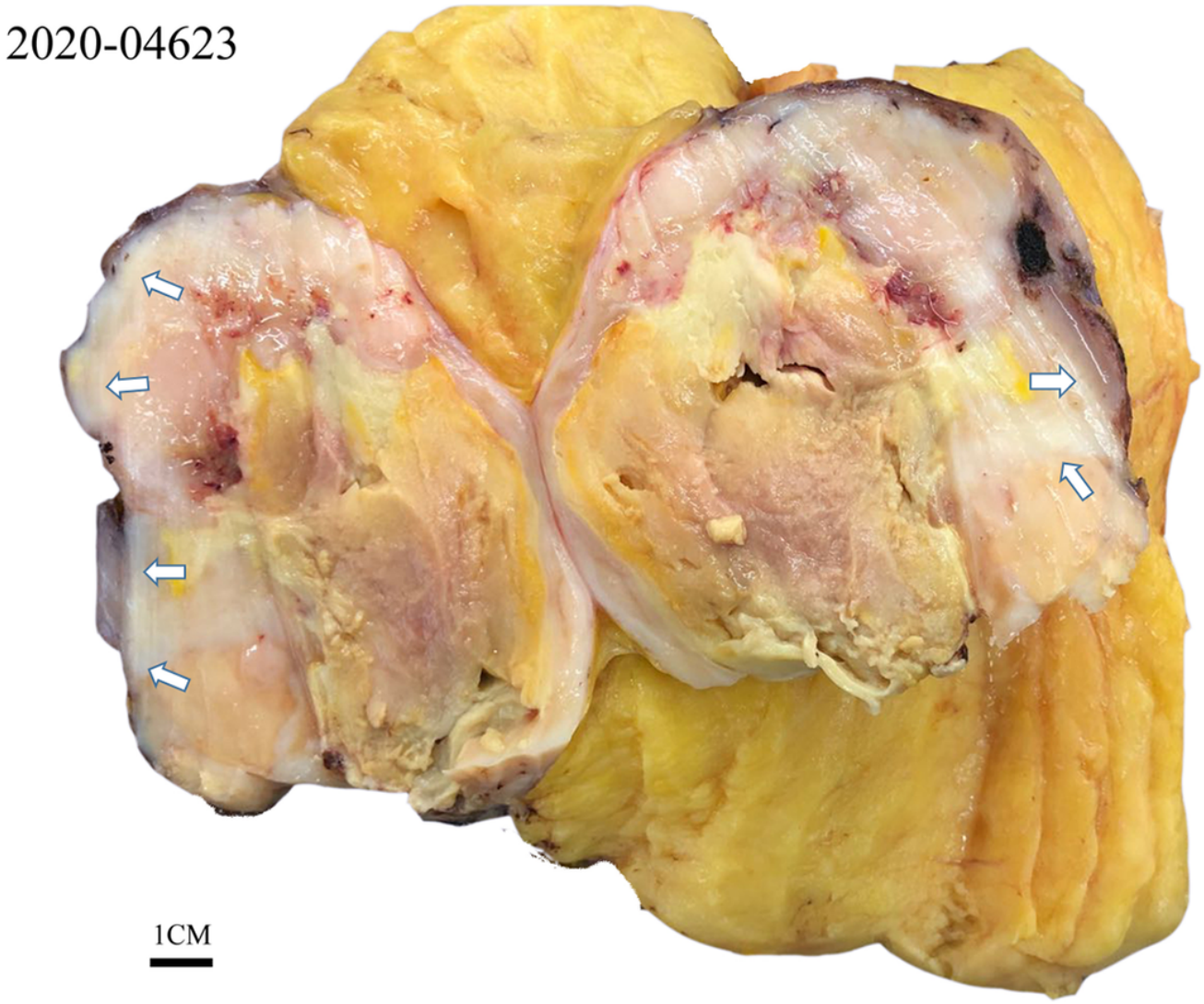

Figure 2

Gross appearance of DDLPS The cross-section of the WDLPS reveals tissue that is yellow, the high-grade DDLPS is fish flesh-colored, and the middle necrotic area is pale yellow; the low-grade DDLPS (white arrows) is grey-white, but the local area is grayish-brown.

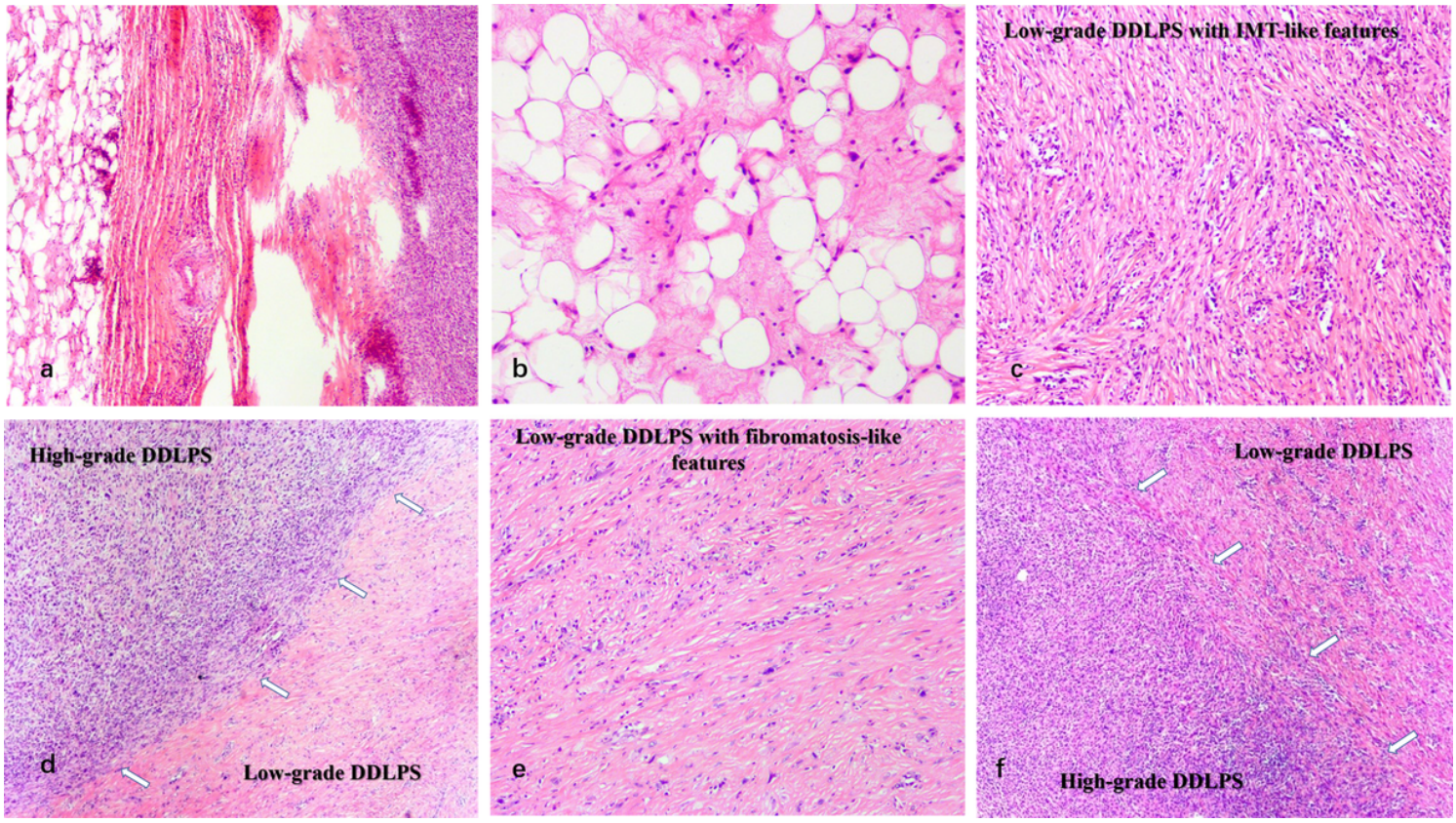

Figure 3

Histologic analysis of DDLPS specimens (a) There is a sudden differentiation between the highly differentiated component and the dedifferentiated component. (Hematoxylin-eosin stain; ×40) (b) Typical well-differentiated liposarcoma of the adipocytic/lipoma-like type. (Hematoxylin- eosin stain; ×100) (c-d) Transition from low-grade dedifferentiation with inflammatory myofibroblastic tumor-like features to high-grade dedifferentiation with undifferentiated pleomorphic sarcoma features. (Hematoxylin-eosin stain; c ×40). The boundary (white arrows) between them is clear. (Hematoxylin-eosin stain; d ×20) (e-f) Transition from low-grade dedifferentiation with fibromatosis-like features to high-grade dedifferentiation with undifferentiated pleomorphic sarcoma features. (Hematoxylin-eosin stain; e×40). The boundary (white arrows) between them is clear. (Hematoxylin-eosin stain; f ×20)

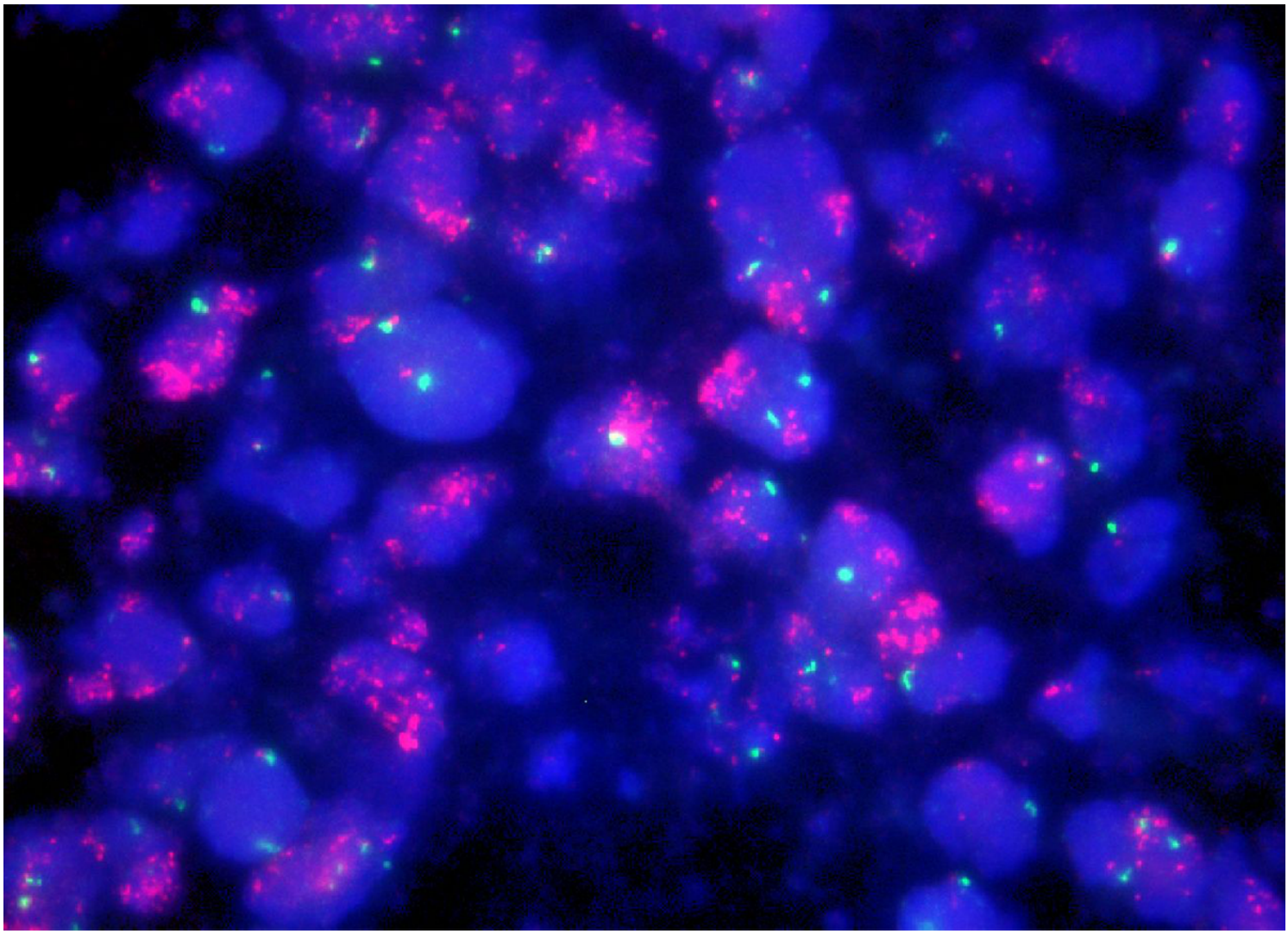

Figure 4

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

Supplementary Files

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