

## Case Report

# Retroperitoneal dedifferentiated liposarcoma with osteosarcomatous components: a case report

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**Abstract:** We report a rare case of recurrent retroperitoneal dedifferentiated liposarcoma with osteosarcomatous components. An 82-year-old male diagnosed with recurrent retroperitoneal liposarcoma underwent a tumor resection. Histologically, osseous matrix with osteoid and mature hyaline cartilaginous tissues with high cellularity were observed in a fibrous background through most of the tumor, and scattered MDM2- and CDK4-positive atypical hyperchromatic stromal cells were detected surrounding the dedifferentiated areas. Dedifferentiation occurs in up to 10% of well-differentiated liposarcomas, frequently resembling a malignant fibrous histiocytoma-like pleomorphic sarcoma. In contrast, divergent differentiation with osteosarcomatous components is considered to be extremely rare.

**Keywords:** Dedifferentiated liposarcoma, osteosarcoma, retroperitoneum

## Introduction

Liposarcomas are rare malignant tumors that account for 0.1% of all malignancies [1]. However, they are one of the most common soft tissue sarcomas, accounting for approximately 15% soft-tissue tumors in adults, and tend to develop in the retroperitoneum and extremities [2]. According to the World Health Organization (WHO) classification of soft tissue sarcomas published in 2002, liposarcomas can be divided into 5 clinicopathological subgroups: well-differentiated liposarcoma (WDL), dedifferentiated liposarcoma (DDL), myxoid liposarcoma, round cell liposarcoma, and mixed-type liposarcoma [3].

Dedifferentiation occurs in up to 10% WDL, including approximately 90% DDL that arise de novo and 10% that develop as recurrences. DDL can be identified histologically by the transition from WDL to nonlipogenic sarcoma, and the dedifferentiated areas demonstrate variable histological characteristics. Most frequently, DDL resembles a malignant fibrous histiocytoma (MFH)-like high-grade pleomorphic sarcoma or an intermediate- to high-grade

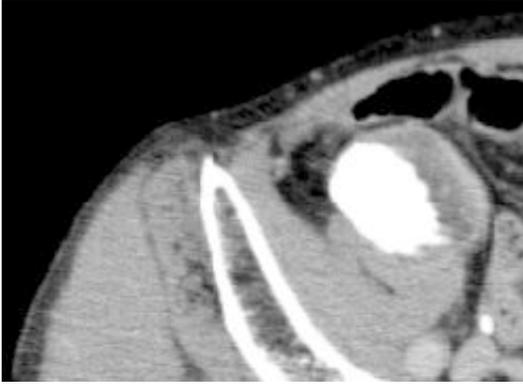
myxofibrosarcoma. In contrast, divergent differentiation, including the development of rhabdomyosarcomatous, leiomyosarcomatous, or osteosarcomatous components, has been reported in less than 5% DDL [4]. In particular, cases of DDL with osteosarcomatous components are considered to be extremely rare.

Here we report a rare case of recurrent retroperitoneal DDL with osteosarcomatous components.

## Case report

An 82-year-old male was referred to our hospital for a right lower abdominal mass. His surgical history included resection of a well-differentiated inguinal retroperitoneal liposarcoma that was performed 6 years ago at another hospital. During physical examination, an immobile solid tumor was palpated in the lower quadrant of his abdomen. Although blood investigations results were normal, abdominal computed tomography (CT) revealed a tumor (3 × 3 cm in size) containing calcification that was located in the dorsal aspect of the ileocecal region (**Figure 1**). Tumor resection was performed, and a diagnosis of

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**Figure 1.** Abdominal computed tomography (CT) revealed a tumor containing calcification located in the dorsal aspect of the ileocecal region.

recurrent retroperitoneal liposarcoma was made. The resected solid tumor was 5 × 5 × 3.5 cm in diameter, which contained calcificated areas inside the tumor that were evident macroscopically (**Figure 2A**). Histologically, osseous matrix with osteoid and mature hyaline cartilaginous tissues with high cellularity were observed in a fibrous background through the most of the tumor (**Figure 2B**). Moreover, adipose tissue with fibrous septa containing scattered atypical hyperchromatic stromal cells were detected surrounding the dedifferentiated area (**Figure 2C**). Immunohistochemistry revealed that all of these scattered atypical stromal cells, as well as some of osteosarcomatous atypical cells were positive for MDM2 (monoclonal, Invitrogen, Carlsbad, CA) and CDK4 (polyclonal, Abcam, Cambridge, UK), which are known to be liposarcoma and low-grade osteosarcoma markers (**Figure 3A, 3B**). Thus, a diagnosis of recurrent retroperitoneal DDL with high-grade osteosarcomatous transformation juxtaposed to the low-grade osteosarcomatous components was confirmed. The patient has remained healthy with no recurrences or metastases for 1 year after resection.

### Discussion

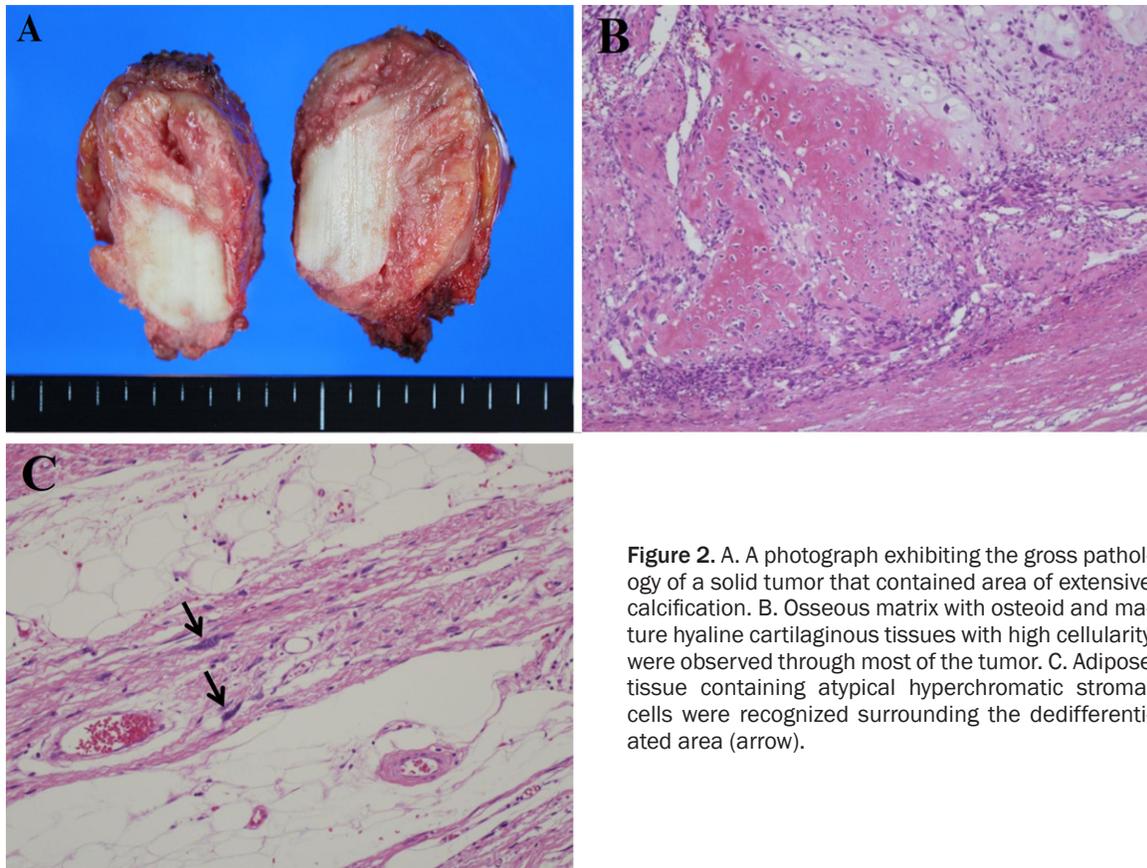
The concept of DDL was first proposed by Evans in 1979 [5]. In general, DDL has been defined as a nonlipogenic neoplasm with WDL juxtaposed to a high-grade malignant fibrous histiocyoma (MFH)-like pleomorphic sarcoma or an intermediate- to high-grade myxofibrosarcoma.

However, less frequently, DDL with divergent differentiations such as rhabdomyosarcomatous, leiomyosarcomatous, or osteosarcomatous components have been observed. Local recurrence, metastasis, and mortality rates of DDL are significantly worse compared with those for pure WDL or myxoid liposarcoma. Dedifferentiation occurs more often in the retroperitoneal space than at other locations, and the metastasis and mortality rates of retroperitoneal DDL (18% and 34%, respectively) are significantly higher compared with those for DDL at other locations (15% and 11%, respectively) [4].

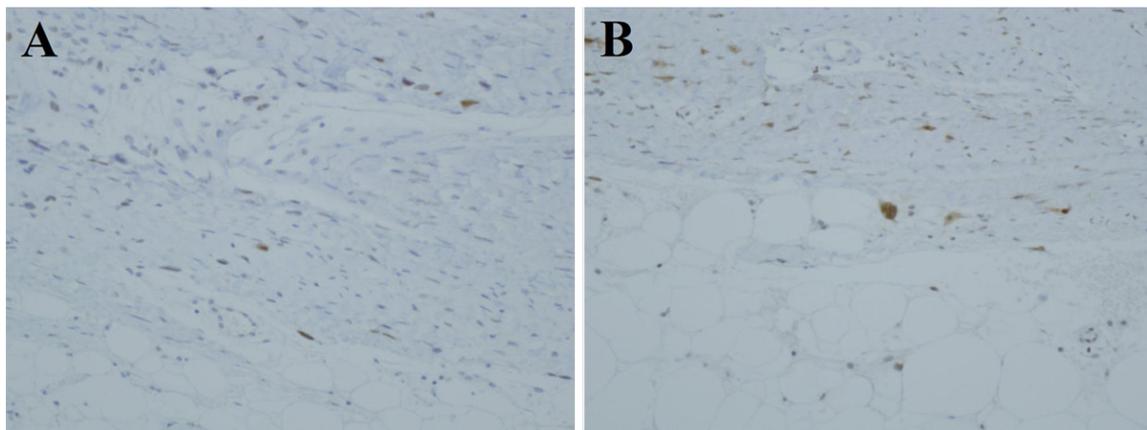
DDL with osteosarcomatous component is defined as a conventional high-grade osteosarcoma that features immature lace-like osteoid production, high cellularity, high nuclear grade, brisk mitotic activity, and necrosis. Because benign reactive or metaplastic bone and cartilage formation can be recognized in the dedifferentiated component of liposarcoma, we should not confuse real osteosarcomatous differentiation with benign ossification. Moreover, recognition of low-grade osteosarcomatous components is important as well because the fibro-osseous component might seem so bland that it could be confused with benign metaplasia [14]. Liposarcomas containing pure low-grade dedifferentiation should not be categorized as DDL on the basis of the traditional classification, but this categorization might be controversial to some extent. Henricks et al. proposed that the definition of DDL should be expanded to include pure low-grade osteosarcomatous differentiation because low-grade areas might be evident alone or in association with high-grade dedifferentiation and exhibit behaviors more similar to traditional DDL than to WDL [4].

By reviewing the literature, we found 9 publications (13 cases) describing tumors that were diagnosed as DDL with high-grade osteosarcomatous components (**Table 1**) [4, 6-13]. The mean age of the patients, excluding case 2 (age was not reported) was 60.6 ± 16.8 years, and the most common tumor sites were the retroperitoneum (6 cases) and thigh (4 cases). To the best of our knowledge, in all the patients who received surgical treatment, the metastasis/recurrence rate was 45%, and the mortality rate was 27%.

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**Figure 2.** A. A photograph exhibiting the gross pathology of a solid tumor that contained area of extensive calcification. B. Osseous matrix with osteoid and mature hyaline cartilaginous tissues with high cellularity were observed through most of the tumor. C. Adipose tissue containing atypical hyperchromatic stromal cells were recognized surrounding the dedifferentiated area (arrow).



**Figure 3.** Scattered atypical hyperchromatic stromal cells around the dedifferentiated area were positive for MDM2 and CDK4. A. Immunohistochemical analyses using anti-MDM2 antibody or (B) anti-CDK4 antibody are presented.

Amplifications of genes *MDM2* and *CDK4*, which are located in the chromosomal subregion 12q13-q15, have been implicated in liposarcoma tumorigenesis [14]. Evaluation of MDM2 and CDK4 expressions by immunohistochemistry and fluorescence in situ hybridiza-

tion (FISH) have become important tools to distinguish WDL from benign adipocytic neoplasms and DDL resulting from other sarcomas. Furthermore, recent studies revealed that MDM2 and CDK4 were overexpressed not only in WDL but also in many low-grade osteosarco-

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**Table 1.** Reported cases of dedifferentiated liposarcoma with high-grade osteosarcomatous components

Case	Year	Author	Age (yr) / Sex	Site	Size (cm)	Primary or secondary	Primary site	Outcome
1	1993	Ippolito et al. [9]	67 / F	Thigh	35	Primary	-	NA
2	1997	Henricks et al. [4]	NA	NA	NA	NA	-	NA
3	2000	Yamamoto et al. [6]	78 / M	Thigh	28	Primary	-	NED, 4yr
4	2000	Hasegawa et al. [7]	57 / M	Retroperitoneum	40	NA	-	DOD, 3yr 9mo
5	2000	Hasegawa et al. [7]	54 / M	Retroperitoneum	16	NA	-	NED, 4yr 8mo
6	2001	Forus et al. [8]	32 / F	Lung	NA	Secondary	Retroperitoneum	DOD, 1yr
7	2003	Toms et al. [11]	78 / F	Buttock	20	Primary	-	NED, 9mo
8	2005	Yu et al. [13]	59 / F	Thigh	11	Primary	-	NED, NA
9	2009	Toshiyasu et al. [12]	50 / M	Retroperitoneum	NA	Primary	-	DOD, 7mo
10	2009	Toshiyasu et al. [12]	54 / M	Retroperitoneum	NA	Primary	-	NED, 2yr
11	2010	Yoshida et al. [14]	55 / M	Thigh	20	NA	-	NED, 11yr
12	2010	Yoshida et al. [14]	69 / F	Axilla	NA	NA	-	AWD, 2yr
13	2010	Yoshida et al. [14]	53 / F	Retroperitoneum	27	NA	-	AWD, 2mo
14	2013	Our case	82 / M	Retroperitoneum	5	Secondary	Retroperitoneum	NED, 1yr

M, male; F, female; NA, data not available; NED, no evidence of disease; AWD, alive with disease; DOD, died of disease.

mas [15]; therefore, low-grade osteosarcoma and WDL might partially share a common genetic background.

### Disclosure of conflict of interest

The authors declare no conflicts of interest.

### Abbreviations

WDL, well-differentiated liposarcoma; DDL, dedifferentiated liposarcoma; MFH, malignant fibrous histiocytoma.

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