# Uterine leiomyosarcoma with osteosarcomatous dedifferentiation

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## Abstract

Leiomyosarcoma is the most common sarcoma of the uterine corpus, however, uterine dedifferentiated leiomyosarcoma remains a poorly characterized entity. Dedifferentiation in leiomyosarcoma can be defined as the occurrence of a high-grade undifferentiated sarcoma in association with a lower-grade sarcoma that demonstrates morphologic and immunophenotypic evidence of myogenic differentiation. The occurrence of extensive heterologous elements in the high-grade area can be problematic confusing the tumor with other more specific types of high-grade sarcomas. Available reports of this entity indicate aggressive biological behavior and poor prognosis. Herein, we describe a case of a 35-year-old woman who presented with menorrhagia and underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy. The histopathological examination of the surgical specimen revealed features of a low-grade leiomyosarcoma juxtaposed to a high-grade sarcoma with osteosarcomatous differentiation.

**Keywords** dedifferentiated; heterologous; leiomyosarcoma; osteosarcomatous differentiation; uterus

## Introduction

The concept of "dedifferentiation" is a well-known phenomenon in sarcoma pathology. It was described in chondrosarcoma in 1971 by Dahlin and Beabout,[1] and since then dedifferentiation has been identified in a variety of other bone and soft tissue sarcomas. The term "dedifferentiation" is used when a high-grade sarcoma, usually with an unrecognizable line of differentiation, develops in association with a pre- or co-existing low-grade sarcoma. The development of dedifferentiation is often heralded by the onset of sudden or rapid increase in tumor size. Morphologically, the low- and high-grade components are juxtaposed next to each other usually (but not always) with a sharp transition. It is important to recognize dedifferentiation histologically as it is an indicator of tumor progression and aggressive biologic behavior.[2,3] Dedifferentiation may arise de novo or upon recurrence.[4]

Dedifferentiated leiomyosarcoma (LMS) is a controversial entity with no consensus regarding its exact definition and whether or not it is biologically distinct from garden-variety pleomorphic LMS. The term pleomorphic LMS is sometimes used for tumors that still retain the expression of smooth muscle markers in the high-grade component while dedifferentiated LMS refers to those tumors that lack immunophenotypic evidence of myogenic differentiation.[3] The first reports of soft tissue dedifferentiated LMS appeared in the early 1980s,[5–7] while the first of a uterine dedifferentiated LMS was likely by Fukuda et al. in 1991 (Table 1).[8] However, it is possible that some prior reports of heterologous uterine sarcomas and mesenchymomas represented heterologous dedifferentiation in LMS.[9] The recent WHO book of soft tissue tumors briefly describes dedifferentiated LMS as a morphological pattern of LMS,[10] but there is no mention of this entity in the WHO book of tumors of female reproductive organs.[11] The dedifferentiated component usually occurs in the form of undifferentiated pleomorphic sarcoma, or what used to be called "MFH-like" sarcoma, although heterologous sarcomatous elements such as osteosarcomatous, rhabdomyosarcomatous and rhabdoid elements may occasionally be seen.[12–14] Accordingly, it is not possible to establish a definite diagnosis of dedifferentiated LMS unless the low-grade area of the tumor with the better myogenic differentiation is identified. Therefore, it is important to ensure that tumor sampling is adequate and representative of the different tumor areas identified grossly. Herein, we report a case of uterine LMS with histological features compatible with dedifferentiated LMS.

## Case summary

A 35-year-old lady who presented with menorrhagia was found to have a large mass arising within the uterine wall on imaging studies. The patient underwent surgery during which an enlarged uterus containing a mass was identified along with tumor deposits involving the omentum and peri-appendiceal region. The uterine mass was sampled for frozen section and the result came back as "atypical spindle cell tumor, sarcoma cannot be ruled out". Aspirated peritoneal fluids later showed malignant cells. The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy, partial omentectomy and appendectomy. The pathological examination of the resected specimen showed an enlarged globular uterus that was distended by an irregular fleshy tan-colored tumor in the anterior uterine wall, 12 cm in maximum dimension, infiltrating the full thickness of the uterine wall with areas of hemorrhage and necrosis (Figure 1). On low-power histological examination, the tumor was hypercellular and infiltrative showing two discernible cell populations: mononuclear cells admixed with numerous multinucleated osteoclast-like giant cells (Figure 2a). The mononuclear cells were spindle to epithelioid growing in sheets and vague fascicular pattern and displaying nuclear pleomorphism, increased mitotic activity up to 30/10 high power field and abnormal mitotic figures (Figure 2b). The giant cells were scattered throughout the tumor but were particularly prominent and back-to-back in some foci with some cells containing more than

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**Previously reported cases of uterine dedifferentiated leiomyosarcoma**

| Author | Year of publication | No. of cases | Age | Histology of "dedifferentiated" component | Extra-uterine spread |
|---|---|---|---|---|---|
| Fukuda T et al.[8] | 1991 | 1 | NA | UPS (MFH-like) and giant cell tumor | NA |
| Patai K et al.[15] | 2006 | 1 | 54 | Malignant giant cell tumor | — |
| Iihara K et al.[16] | 2007 | 1 | 48 | UPS (MFH-like) | Lung and brain |
| Chen E et al.[4] | 2011 | 2 | 59 & 80 | UPS (MFH-like) | — |
| Rawish KR et al.[17] | 2012 | 1 | 48 | Osteosarcoma | Pelvis and intra-peritoneal |
| Anh Tran T et al.[18] | 2012 | 1 | 80 | Osteosarcoma, chondrosarcoma, liposarcoma-like, giant cells | Lung and pelvis |
| Parikh P et al.[19] | 2015 | 2 | 60 & 38 | Osteosarcoma | NA |

UPS = undifferentiated pleomorphic sarcoma; MFH = malignant fibrous histiocytoma; NA = not available.

**Table 1**

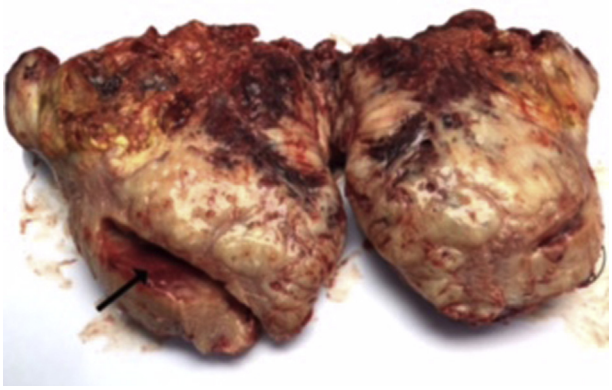

**Figure 1** Gross appearance of the uterine tumor. The tumor is irregular and fleshy invading the full thickness of the uterine wall (the arrow points to the endometrial cavity).

100 nuclei ("giant" giant cells) imparting a look that is reminiscent to giant cell tumor of bone (Figure 2c, d). There were even foci showing cystic spaces containing giant cells in their walls resembling secondary aneurysmal bone cyst changes (Figure 2e). Upon close inspection, malignant osteoid matrix production was identified deposited in a lacy trabecular pattern with focal calcification compatible with osteosarcomatous differentiation (Figure 2f). Lymphovascular invasion was identified. Following a thorough search, abrupt transition into a different looking area was seen in one slide. This area constituted <5% of the tumor and was composed of a lower-grade spindle cell sarcoma with cigar-shaped nuclei arranged in interlacing fascicles in keeping with conventional leiomyosarcoma (Figure 3a). Immunohistochemical studies performed on the low-grade component revealed diffuse positivity for smooth muscle actin and h-caldesmon (Figure 3b) and focal positivity for desmin while the high-grade component showed only focal equivocal positivity for all three myogenic markers. After thorough sampling of the tumor and exclusion of primary skeletal osteosarcoma clinically, a final diagnosis of "dedifferentiated leiomyosarcoma of the uterus with heterologous osteosarcomatous differentiation" was rendered. The uterine cervix and adnexae were spared but the separately submitted peri-appendiceal and omental deposits proved to be metastatic tumor deposits histologically.

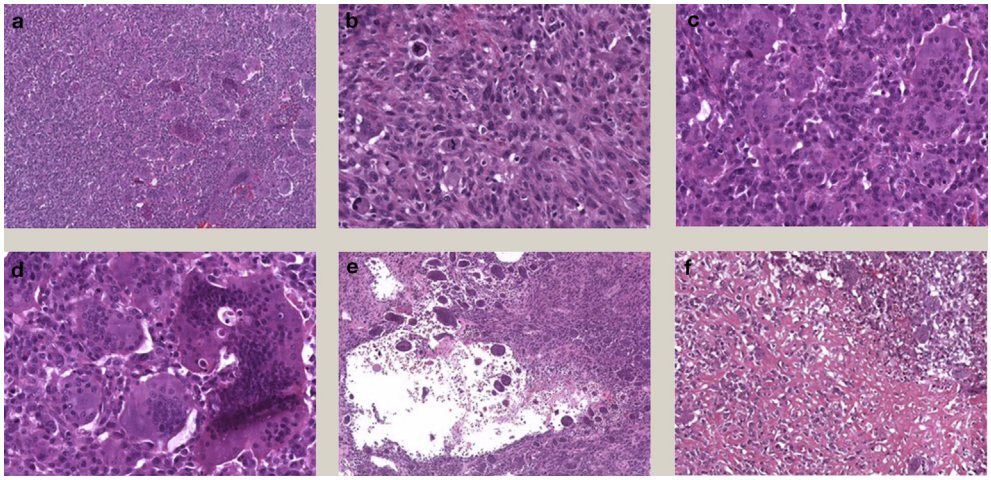


**Figure 2** Histopathology of the high-grade component of the tumor. (**a**). At scanning power, the tumor shows mononuclear cells admixed with multinucleated giant cells. (**b**). The mononuclear cells grow in sheets and vague fascicular pattern and display nuclear pleomorphism and increased mitotic activity (×20 mag). (**c**). Back-to-back osteoclast-like giant cells reminiscent to giant cell tumor of bone (×20 mag). (**d**). "Giant" giant cells with >100 nuclei per cell reminiscent to giant cell tumor of bone (×20 mag). (**e**). Aneurysmal bone cyst-like changes (scanning mag). (**f**). Osteosarcomatous differentiation (scanning mag).