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Case Report

Multiple Recurrent Atypical Lipomatous Tumors/Well-Differentiated Liposarcomas and Dedifferentiated Liposarcomas Treated with Multiple Surgical Resections: A Case Report

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Keywords
Atypical lipomatous tumor · Well-differentiated liposarcoma · Dedifferentiated liposarcoma · Multiple liposarcoma · Multicentric liposarcoma

Abstract
Atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLPS) is usually a solitary adipocytic tumor. ALT/WDLPS shows no potential for metastasis unless it undergoes dedifferentiation. No case of multiple ALT/WDLPS has been reported in recent years. We present a rare case of multiple recurrent liposarcomas. A 71-year-old man with a history of scrotal ALT/WDLPS at 61 years presented with multiple large tumors spread throughout the body. The patient was bedridden and severely limited in his activities of daily living (ADL) due to multiple large tumors in the trunk and lower extremities. Radiological examination revealed multiple adipocytic tumors, mainly in the soft tissues of the trunk and extremities, with several visceral lesions. Tumors were resected in stages, starting with large tumors directly related to disability. Repeated palliative resections improved the patient's ADL; he regained ambulation and was discharged 18 months after admission. Twelve surgeries were performed to remove 44 adipocytic tumors from the testis, left chest wall, perigastric area, ileum, left inguinal region, both buttocks, thighs, and lower legs. Histological examination revealed dedifferentiated

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components in five tumors, while 39 tumors were diagnosed as ALT/WDLPS. At the age of 76 years, the patient developed an unresectable dedifferentiated liposarcoma between the heart and aorta, leading to fatality at 79 years. The patient's clinical course suggested multiple metastases of ALT/WDLPS of scrotal origin or ALT/WDLPS of multicentric origin. Although multicentric ALT/WDLPS or ALT/WDLPS metastases are rare, they should be considered when multiple large adipocytic tumors are found throughout the body. Despite the presence of numerous large malignant tumors, surgical treatments of the lesions can improve ADL and prolong life if the tumors are of low-grade malignancy.

Introduction

Atypical lipomatous tumor (ALT)/well-differentiated liposarcoma (WDLPS) accounts for approximately half of all liposarcomas [1] and develops predominantly in the extremities and retroperitoneum [2]. Local recurrence is reported to occur in approximately 30–50% of cases, with metastasis rarely occurring [3]. Approximately 10% of all ALT/WDLPS cases may exhibit dedifferentiation [3], indicating the importance of being aware of their metastatic potential. Notably, the frequency of metastasis in dedifferentiated liposarcomas has been reported to be 15–30% [4]. ALT/WDLPS does not usually have metastatic potential; however, previous reports have indicated it may present as multiple tumors with a frequency of 2% [5, 6]. However, these reports were published in the 1940s and 1950s, and no case of multiple ALT/WDLPS has been reported in recent years. Herein, we report an extremely rare case of multiple liposarcomas, most of which were diagnosed as ALT/WDLPS, occurring in the soft tissue of the entire body following primary scrotal ALT/WDLPS.

Case Presentation

The male patient in the case report was healthy until he was first diagnosed with scrotal ALT/WDLPS and underwent surgery at the age of 61 years. He had no remarkable familial histories besides his father's history of gastric cancer. At 63, the patient was aware of an enlarging mass in his left lower leg but ignored it. At 71, he was brought to our hospital as an emergency case of malnutrition, dehydration, and inability to ambulate. Physical examination revealed multiple large masses throughout his body, including the bilateral thighs, legs, and left chest wall. The patient was bedridden (Eastern Cooperative Oncology Group Performance Status [PS] 4), with limitations in physical movement due to the large tumor size. Computed tomography (CT) revealed multiple adipocytic lesions in the chest wall, bilateral groins, thighs, lower legs, perigastric tissue, and ileocecal region (shown in Fig. 1). The patient was admitted to our hospital for intravenous treatment for malnutrition, dehydration, and rehabilitation, which improved his general condition over 4 months. However, his activities of daily living (ADL) were severely restricted due to the multiple large tumors. We decided not to perform chemotherapy because the patient was elderly, had a low PS, and the benefit of chemotherapy for ALT/WDLPS is limited. Since the tumors had not metastasized to the vital organs, such as the lungs, we judged that tumor volume reduction could improve the patient's general condition and survival. The tumors were resected sequentially, starting with large tumors in the thighs that were related to the patient's ADL and disability. In the first surgery, six tumors weighing 17 kg were resected from the right thigh (shown in Fig. 2). Additionally,

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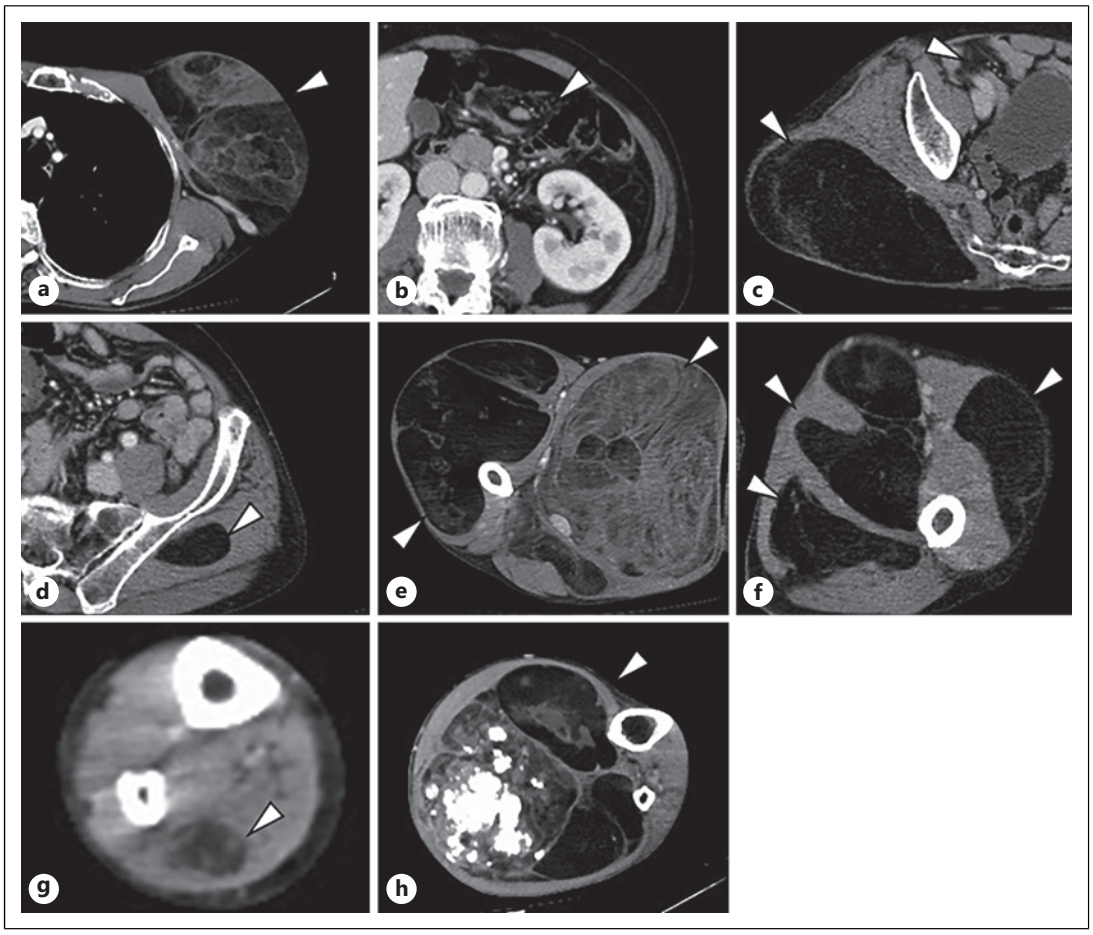

Fig. 1. CT images at the initial visit. Tumors were observed on the left chest wall (**a**), perigastric area (arrow) (**b**), ileocecal area (arrow) and right buttock (**c**), left buttock (**d**), right thigh (**e**), left thigh (**f**), right lower leg (**g**), and left lower leg (**h**). Multiple ossifications were found in the tumor on the left lower leg. CT, computed tomography.

tumors in the buttock and left chest wall, inguinal wall, thigh, and lower leg were resected in three operations. Eighteen months after admission, the patient regained the ability to walk with a cane and was discharged. In total, twelve surgeries were performed to remove 44 adipocytic tumors from the testis, left chest wall, perigastric area, ileum, left inguinal region, both buttocks, thighs, and lower legs (Table 1). Radiological images of the primary scrotal liposarcoma from another hospital were unavailable; however, a review of histopathological specimens from the initial surgery revealed no obvious dedifferentiated components (shown in Fig. 3a). Histopathological analyses of the resected tumors revealed that only five specimens had dedifferentiated components in four locations: the left lower leg (two surgeries), perigastric tissue (shown in Fig. 3b), right lower leg, and left thigh, with the remaining specimens being ALT/WDLPS. In the first surgical specimen from the left lower leg, a grayish-white, dedifferentiated component was seen in approximately 5% of the tumor. Ossifying lesions were found within a well-differentiated component of this tumor and were considered to indicate metaphyseal changes within an ALT/WDLPS rather than osteosarcomatous dedifferentiation because the bone formation pattern did not appear to be neoplastic and numerous nodules were present. The perigastric tumor showed two distinct images: histology that corresponded to ALT/WDLPS and a dedifferentiated component with myxoid

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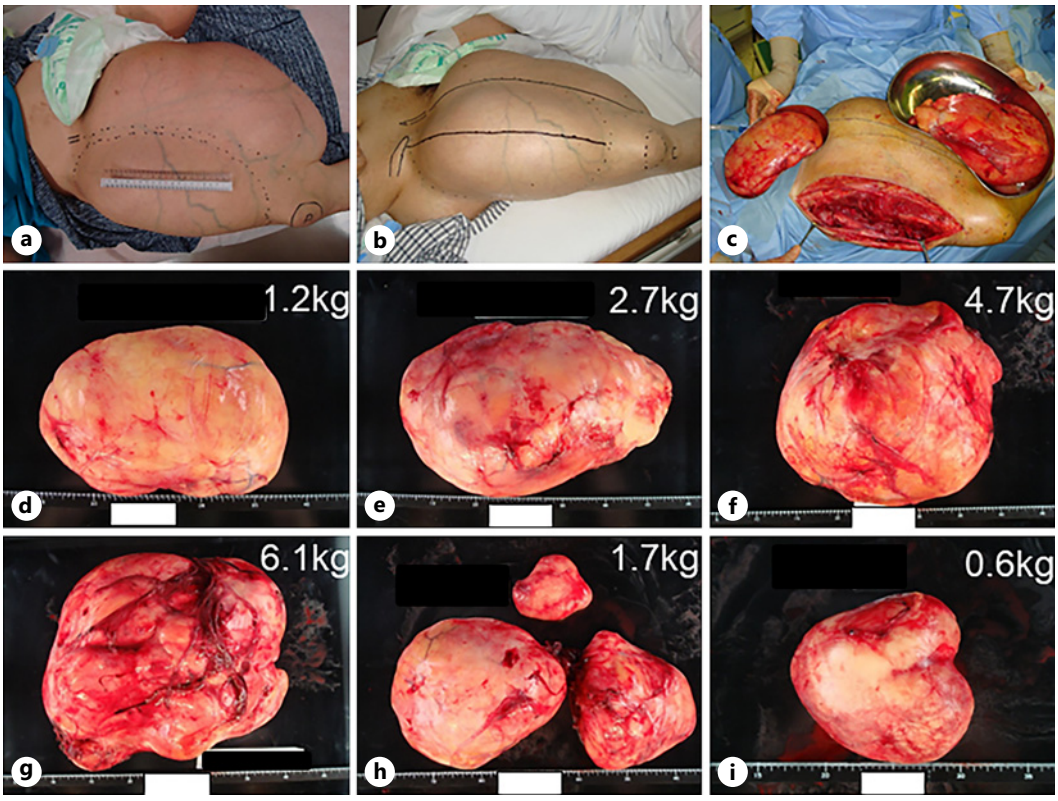

Fig. 2. Surgical findings. Six tumors, weighing 17 kg in total, were resected. Preoperative (**a**, **b**) and intraoperative findings (**c**). Tumors were resected from the sartorius (**d**), vastus intermedius (**e**), adductors (**f**), distal and proximal hamstrings (**g**, **h**), and popliteal fossa (**i**).

liposarcoma-like histology. Fluorescence in situ hybridization for *MDM2* and *DDIT3* in the perigastric tumor revealed *MDM2* amplification (shown in Fig. 3c) without *DDIT3* translocation. Therefore, a diagnosis of dedifferentiated liposarcoma was reached. Although the proportion of dedifferentiated components tended to increase over time, most of the tumors were diagnosed as ALT/WDLPS and predominantly exhibited a well-differentiated component (Table 1).

A follow-up CT at age 76 years revealed an adipocytic tumor in the posterior mediastinum with suspected dedifferentiation. The tumor in the posterior mediastinum was large and adjacent to the heart and aorta, making it unresectable. At 78, he was brought to the hospital using an ambulance with complaints of respiratory distress 7 months after the final surgery for the resection of adipocytic tumors in the right buttock and left thigh. CT scan revealed marked enlargement and progression of the posterior mediastinal tumor, with numerous adipocytic tumors in the left lung and subcutaneous, intramuscular, retroperitoneal, and pelvic regions. The best supportive care policy was assured, with no provision of life-prolonging treatment, and the patient died of advanced disease 3 days after emergency admission.

Discussion

Overall, we encountered a case of primary scrotal ALT/WDLPS that recurred as multiple liposarcomas; 44 adipocytic tumors were removed after 12 surgeries, 39 of which were ALT/WDLPS. The patient's ADL improved with only surgical resection of adipocytic tumors in the

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Table 1. Description of surgically removed tumors

Surgery	Age, years	Location	Mass, kg	Size, cm	Tumors, *n*	Pathological findings	Dedifferentiated components, %
1	61	Testis	NA	NA	1	WD	NA
2	71	Right thigh	17	8–30	6	WD	0
3	71	Right buttock,	4.3	16	1	WD	0
		left chest wall		23	1	WD	0
4	71	Left inguinal lesion, left thigh, left lower leg	7.8	14–30	6	WD (left inguinal lesion, left thigh), DD (left lower leg)	5
5	73	Left buttock, left popliteal lesion	NA	14–16	3	WD	0
6	74	Right lower leg, right inguinal lesion	1	8–14	3	WD	0
7	75	Gastric area, ileocecal lesion	NA	4–10	2	DD (gastric area), lipoma (ileocecal lesion)	10
8	75	Left thigh, left lower leg, right buttock	NA	9–23	7	WD (left thigh, right buttock), DD (left lower leg)	80
9	75	Right lower leg	NA	21	1	DD	95
10	76	Right thigh	NA	24	1	WD	0
11	77	Right thigh	NA	3–24	7	WD	0
12	78	Right buttock, left thigh	4.9	13–21	5	WD (right buttock), DD (left thigh)	20

WD, well-differentiated liposarcoma; DD, dedifferentiated liposarcoma; NA, not available.

extremities, trunk, and gastrointestinal lesions, after which he was followed up for 8 years after his initial visit. The patient's clinical course suggested multiple metastases of ALT/WDLPS of scrotal origin, but we could not rule out ALT/WDLPS of multicentric origin or multiple recurrences of distant secondary dedifferentiated liposarcoma.

Multiple liposarcomas were first described by Ackerman [5] in 1944. ALT/WDLPS are solitary, and multiple tumors have only been reported in 2% of cases in previous studies [6, 7]. Some of these multiple tumor cases have been reported to be multicentric. However, these reports were published in the 1940s and 1950s, and no cases of multiple ALT/WDLPS have been reported in recent years. The diagnostic concept of multicentric liposarcoma is defined as follows: (1) the site of origin is the preferred site of liposarcoma; (2) there are no tumors in the lungs, liver, or bones, which are the preferred metastatic sites; (3) the histological type is either well-differentiated or myxoid; (4) the intervals are long in cases of heterochrony; and (5) a lipoma may be present [5, 8]. Despite this, no clear diagnostic criteria yet exist to determine whether a tumor is metastatic or multicentric. Subsequently, we reviewed multicentric ALT/WDLPS cases and identified only three with detailed descriptions (Table 2)

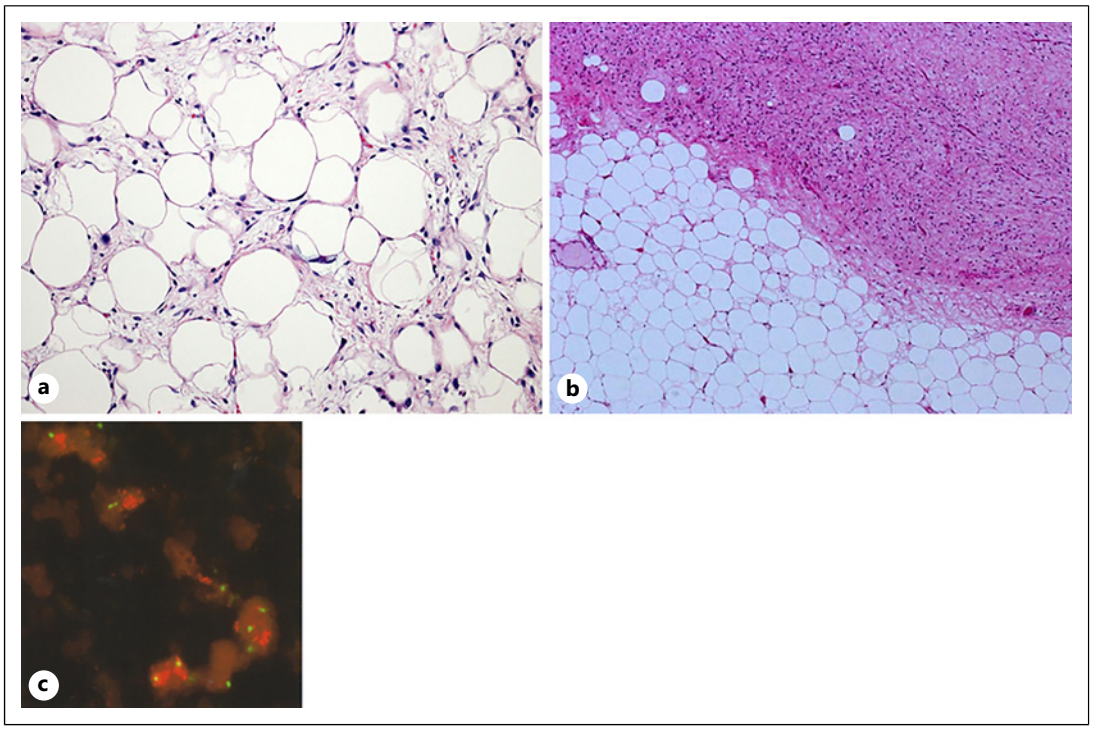

Fig. 3. Pathological and FISH findings of resected specimens. **a** Histopathological findings of the scrotal tumor (H&E, ×100). No obvious dedifferentiated components were observed. **b** Histopathological findings of the perigastric tumor included two images corresponding to ALT/WDLPS and a dedifferentiated component with myxoid liposarcoma-like histology (H&E, ×40). **c** FISH findings in the perigastric tumor revealed *MDM2* amplification (red).

Table 2. Review of previously reported multicentric, WDLPS cases

Author, year	Age	Sex	Location	Tumors, *n*	Treatment	Follow-up, years	Outcome
Georgiades et al. [9] (1969)	49	F	Thigh, chest wall, lumbar muscles, buttock, forehead, mediastinum, shoulder	12	Surgery	9	AWD
Seenu et al. [8] (1995)	60	M	Mesentery, omentum, retroperitoneum	100<	Surgery Chemotherapy Radiotherapy	1	AWD
Sato et al. [10] (2004)	72	M	Retroperitoneum	3	Surgery	1	CDF

AWD, alive with disease; CDF, continuous disease-free.

[8–10]. Two of the three cases involved the retroperitoneum, with more than 100 tumors, while the other involved the limbs and trunk, with 12 tumors. The retroperitoneal case with more than 100 tumors was treated with radiation, chemotherapy, and surgery, while the remaining cases were only treated surgically. All patients had a good postoperative

course. Because most of the tumors in our case were ALT/WDLPS, surgical treatment was effective, as in previous cases of multicentric ALT/WDLPS. Furthermore, repeated palliative marginal resections prolonged the patient's life for 8 years while maintaining ADL. The present case had the largest number of adipocytic tumors among cases treated with surgery alone.

Regarding liposarcoma metastasis, ALT/WDLPS does not usually metastasize; however, other liposarcomas, such as myxoid, pleomorphic, and dedifferentiated liposarcomas, have metastatic potential [11]. Specifically, the frequency of metastasis in ALT/WDLPS is reported to be approximately 0.1% [12], whereas the metastatic frequency of dedifferentiated liposarcomas is approximately 15–30% [4]. In particular, the lungs are often the sites of dedifferentiated liposarcoma metastases [13]. Soft-tissue metastasis of dedifferentiated liposarcoma has been infrequently reported, with an incidence of approximately 1% [11, 14, 15]. There are no detailed case presentations of soft-tissue metastasis of dedifferentiated liposarcoma. Hence, if we consider the patient as a case of soft-tissue metastasis, this report is the first description of such a case. However, the primary scrotal lesion in this case was ALT/WDLPS, and most of the multiple lesions were low-grade ALT/WDLPS. Therefore, it would be unusual to assume that the secondary dedifferentiated lesions metastasized. Systemic metastases without dedifferentiation, although rare, have been reported in osteosarcoma [16]. Similarly, the multiple lesions in the present liposarcoma case may indicate metastases without dedifferentiation.

Surgical resection is the mainstay treatment for ALT/WDLPS and dedifferentiated liposarcomas [3]. The procedure has a 5-year overall survival rate of 93%, and a long-term prognosis is expected if complete resection is performed for single lesions in patients with ALT/WDLPS [3]. The surgical treatment comprised repeated marginal resection; however, our patient lived for 8 years after the first visit while recovering and preserving postoperative function.

Conclusion

Although multicentric ALT/WDLPS or ALT/WDLPS metastases are rare, they should be considered when multiple large adipocytic tumors are found throughout the body. In the present case, most tumors were low-grade adipocytic tumors, and palliative marginal resections were effective in improving the patient's ADL and prolonging life. The CARE checklist has been completed by the authors for this case report and attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000534181).

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Statement of Ethics

This study was approved by the Ethics Committee of the Keio University School of Medicine (20160298). The patient provided signed informed consent for an Institutional Review Board-approved protocol for research use of medical records, pathologic specimens

obtained as part of routine clinical care, and publication. Written informed consent was obtained from the patient for publication of the details of their medical case and accompanying images prior to their passing away.

Conflict of Interest Statement

The authors declare that they have no competing interests.

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Author Contributions

A.M. and T.H. performed the data analysis and prepared the initial draft of the manuscript. T.H. and R.N. contributed to manuscript writing. T.H. provided final approval of the manuscript. A.M., T.H., S.Y., T.M., N.A., K.K., K.H., K.T., R.N., M.N., and M.M. read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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