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Atypical lipomatous tumor of the hand with transformation to dedifferentiated liposarcoma: a case report

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Abstract

Atypical lipomatous tumor/well-differentiated liposarcoma is the most common sarcoma of soft tissue in adults. We describe the clinical, radiologic, and pathologic features of an atypical lipomatous tumor arising within the soft tissue of the left hand of a 68-year-old female that underwent transformation to dedifferentiated liposarcoma and eventually metastasized. At initial presentation, imaging demonstrated an extensively calcified fatty soft tissue mass with displacement of the digits. Following biopsy and staged debulking, the patient subsequently developed local recurrence, dedifferentiation, and widespread metastases to the lungs, pancreas, bone, and soft tissues. To our knowledge, this is the first case of a cytogenetically proven atypical lipomatous tumor of the hand that has undergone dedifferentiation with widespread metastases.

Keywords

Liposarcoma; Hand; Dedifferentiated; CT; MRI; PET; Metastases

Introduction

While conventional lipomas are the most common mesenchymal neoplasm in adults and liposarcoma the most common soft tissue sarcoma in adults; both are relatively rare in the hand. Atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDL) represent the most common type of malignant adipocytic tumors, accounting for approximately 40–45% of all liposarcomas. They are classified as locally aggressive malignancies with a tendency to recur but without metastatic potential occurring most frequently in the deep soft tissue of the thigh, followed by the retroperitoneum, paratesticular region, and mediastinum [1]. These lesions are characterized by MDM2 and CDK4 gene amplifications at ch12q13–15.

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Conflict of interest The authors declare that they have no conflict of interest.

Dedifferentiation occurs when a primary or recurrent ALT/WDL shows foci of non-lipogenic sarcomatous histology, either high or low grade, which can occur in less than 2% of lesions in the limbs, but probably greater than 20% in the retroperitoneal tumors [1]. The most worrisome clinical feature of dedifferentiated liposarcoma is its predilection for distant metastasis, seen in up to 20% of cases [1]. There are rare case reports of atypical lipomatous tumor [2, 3] and well-differentiated spindle cell liposarcoma of the hand [4, 5]. Thus far, no cases of dedifferentiated liposarcoma of the hand, with or without metastases, have been described. We present the clinical, radiologic, and pathologic findings of a long-standing ALT of the hand with MDM2 gene amplification by fluorescence in situ hybridization (FISH) and SNP-array analysis evolving over the course of 13 years with transformation to dedifferentiated liposarcoma and widespread distant metastases.

Case report

A 68-year-old right hand-dominant female patient was referred to our institution with a 10-year history of a left hand soft tissue mass. The lesion was painless and when first noticed was the size of a dime and did not impact function. Seven years earlier, the patient presented to an outside institution. The initial radiograph and MRI from the outside institution at that time revealed a multinodular lipomatous mass containing peripheral and curvilinear ossification (Fig. 1), and the patient declined surgical amputation. In subsequent years, the nodules grew resulting in difficulty with grip and numbness in the middle finger, and the patient noted a 30-pound weight loss, which prompted her to seek medical attention again. On physical examination (Fig. 2a), the patient had an exophytic multi-nodular mass involving the hand spanning 18 cm in maximum dimension, predominantly extending along the palm of the hand involving multiple web spaces. A radiograph of the left hand (Fig. 2b) confirmed the increase in size, number, and ossification of the nodules involving the entire hand. Surgical biopsy was performed, and histology (Fig. 3a) showed a lipomatous neoplasm consisting of adipocytes of varying shapes and sizes with intervening fibrous septae containing rare atypical hyperchromatic and focally multinucleated cells. There were additional foci of benign cartilage and bone with normal marrow elements representing osteocartilaginous metaplasia (Fig. 3b). Fluorescent in situ hybridization studies (FISH) (Fig. 4a) showed amplification of the MDM2 gene, and SNP-array analysis showed copy number gain of 12q12–12q24.23 with amplification of CDK4 and MDM2 genes confirming the FISH findings. In addition, SNP array showed an additional amplicon at 3q11.2, which involved Ephrin receptor A (Fig. 4b). These findings confirmed the diagnosis of an atypical lipomatous tumor. Due to disabling mass effects, the patient underwent partial excision as part of a staged debulking of the mass.

On the follow-up visit 2 months later, there was new swelling of the palmar aspect of the hand in the region of the fourth digit associated with focal skin breakdown as well as an approximately 1.5-cm freely mobile subcutaneous mass in the anterior ipsilateral mid arm. Open biopsy of the new palmar swelling was performed and showed a high-grade spindle cell sarcoma consistent with dedifferentiated liposarcoma (Fig. 5).

The patient underwent follow-up imaging studies. Radiograph of the left hand (Fig. 6a) 1 year after staged debulking showed increased central and denser ossification along the distal

third and fourth rays corresponding to the swelling on physical examination. MRI of the left hand (Fig. 6b, c) in the same month showed a substantial increase in the non-lipomatous nodules at the palmar aspect of the distal hand widening web spaces. MRI of left arm (Fig. 6d) confirmed a 1.6 × 1.2-cm subcutaneous nodule contacting the cephalic vein in the mid arm. CT of the chest (Fig. 6e) was performed for staging and showed bilateral non-calcified sub-centimeter lung nodules. Positron emission tomography (PET) (Fig. 6f) performed a few days after CT chest showed that the lung nodules, left subpectoral node, left mid arm nodule, and left-hand masses were FDG avid.

The patient underwent a triple ray amputation of the left third through fifth digits and excision of a 1.6-cm subcutaneous mid-arm nodule. The triple ray resection specimen showed a dedifferentiated liposarcoma showing divergent osteosarcomatous morphology arising in a background of atypical lipomatous tumor without involvement of the underlying phalanges (Fig. 7). Mitotic activity was brisk (>10/10 high power fields), and geographic tumor type necrosis was present. The excision specimen of the left mid-arm nodule showed a benign reactive lymph node.

Follow-up CT chest showed an increase in the size and number of pulmonary nodules (not shown). Despite two cycles of gemcitabine and docetaxel, pulmonary nodules increased in size and number. CT-guided biopsy of a lung nodule confirmed metastatic high-grade dedifferentiated liposarcoma with osteosarcomatous differentiation. The patient continued to have progression of disease, with radiologic evidence of diffuse subcutaneous, intramuscular, pancreatic, and peritoneal spread of disease within 1.5 years in the subsequent CT chest, abdomen and pelvis (Fig. 8). The patient was alive with progression of her disease 3 years after her initial presentation in our institution.

Discussion

Dedifferentiated liposarcoma (DDLs) represents histologic progression of an atypical lipomatous tumor/well-differentiated liposarcoma, either primarily or through recurrence, to a sarcoma, usually non-lipogenic, of variable histologic grade [6]. This phenomenon is felt to be time dependent and is related to the efficacy of complete initial resection [7]. Both ALT/WDL and DDLs carry a common genetic driver event characterized by amplification of CDK4 and MDM2 genes located at 12q13–15 [8]. While ALT/WDL shows no potential for distant metastasis, dedifferentiated liposarcoma has been shown to metastasize in 15–20% of cases [6].

In the current literature, there have been no reports of a dedifferentiated liposarcoma or metastases from primary lipomatous neoplasms of the hand. Cribb et al. described ten large lipomatous neoplasms of the upper extremity including five in the hand. Of those five lesions, two were diagnosed as well-differentiated liposarcoma/atypical lipomatous neoplasm based on typical histologic features [2]. An additional case of a 7-cm atypical lipomatous tumor of the hand was reported by Ogose et al. [3]. Other malignant lipomatous tumors reported in the hand include two well-differentiated spindle cell liposarcomas by Mentzel and Deshmukh [4, 5]. In Mentzel's subsequent series of six cases, one occurred in

the back of the hand and all six cases were cytogenetically proven to show deletion of RB1, a hallmark of spindle cell lipoma/spindle cell liposarcoma [9].

The presence of both a benign and malignant mineralized bony matrix as well as a chondroid matrix have been described in lipomatous neoplasms. In benign lesions, mineralization is typically associated with fat necrosis [10]. Rare cases of ossifying lipoma have been described; they generally show lobules of mature adipose tissue intimately associated with benign bone and cartilage [11]. In liposarcomas, chondroid and osseous heterologous components have been reported in myxoid liposarcoma. Both components demonstrate DDIT3 gene rearrangements characteristic of this neoplasm and are considered metaplastic change rather than dedifferentiation [12]. Similarly, we believe that the osteocartilaginous differentiation seen at initial biopsy of our case represents metaplastic change and not dedifferentiation. The presence of normal marrow elements associated with the osteocartilaginous differentiation also supports a metaplastic phenomenon. The initial radiograph in our patient showed multiple calcifications that were peripheral and curvilinear in the masses. This pattern was unusual for fat necrosis, which is typically focal and variable in shape, being spiculated to coarse, and is more consistent with ossification. Calcifications in osteosarcomatous dedifferentiated tumors are usually central and dense, while those in chondrosarcomatous dedifferentiated tumors are distributed as rings and arcs. This supports the pathologic diagnosis of osteocartilaginous differentiation at initial biopsy. In the follow-up radiograph, the calcifications were denser and central, in line with the osteosarcomatous dedifferentiation in the triple-ray amputation specimen.

While morphologic heterogeneity of high-grade sarcomas in DDLPS is well recognized, the tumors frequently resemble pleomorphic undifferentiated sarcoma or high-grade myxofibrosarcoma [13]. In addition, heterologous dedifferentiation is seen in approximately 5–10% of cases in the form of osteosarcomatous/chondrosarcomatous/myogenic and including angiosarcomatous dedifferentiation [14]. A recent case report by Zajicek et al. described an ALT/WDL of the proximal thigh, which showed multiple local recurrences and eventually dedifferentiated, showing a low-grade osteosarcomatous dedifferentiation. FISH studies performed on both the liposarcomatous and osteosarcomatous areas showed MDM2 and CDK4 gene amplification [15]. While our patient had a rapid course with metastases, the histologic types of dedifferentiated components are not known to be independent predictors of outcome [6]. Of additional interest is the 3q11.2 amplicon involving the Ephrin receptor 6 (EPHA6) gene by SNP array analysis of the initial ALT/WDL. Kanojia et al. [16] studied 86 samples of liposarcomas using SNP array and whole exome sequencing analysis and showed consistent amplification of 12q13–15, and other broad and focal amplifications of 1q, 6q, 8q, 11p, 12q, 14q, and 15q, but no amplification of 3q11.2. One could speculate this previously undescribed 3q11.2 amplicon seen in our case may be unique to WDL of the hand and an indicator of aggressive behavior; however, this needs confirmation with additional cases and functional studies.

References

1. Fletcher CDM, Bridge JA, Hogendoorn PCW. In: Mertens F, editor. World Health Organization classification of tumours. Pathology and genetics of tumours of soft tissue and bone. Lyon: IARC Press; 2013 p. 33–8.

2. Cribb GL, Cool WP, Ford DJ, Mangham DC. Giant lipomatous tumours of the hand and forearm. *J Hand Surg (Br)*. 2005;30(5):509–12. [PubMed: 15992974]
3. Ogoe A, Kobayashi H, Morita T, Hasegawa K, Hirata Y. Well-differentiated liposarcoma of the hand. *Scand J Plast Reconstr Surg Hand Surg*. 2000;34:185–7. [PubMed: 10900638]
4. Mentzel T, Toennissen J, Rütten A, Schaller J. Palmar atypical lipomatous tumour with spindle cell features (well-differentiated spindle cell liposarcoma): a rare neoplasm arising in an unusual anatomical location. *Virchows Arch*. 2005;446:300–4. [PubMed: 15719245]
5. Deshmukh SD, Gulati HK, Yadav P, Naik P. Palmar well differentiated spindle cell liposarcoma: presentation of a rare tumor at a rare site. *Hand Surg*. 2013;18(1):115–20. [PubMed: 23413865]
6. Henricks WH, Chu YC, Goldblum JR, Weiss SW. Dedifferentiated liposarcoma: a clinicopathological analysis of 155 cases with a proposal for an expanded definition of dedifferentiation. *Am J Surg Pathol*. 1997;21(3):271–81. [PubMed: 9060596]
7. Goldblum JR, Weiss SW, Folpe AL. *Enzinger and Weiss's soft tissue tumors*. 6th ed. Philadelphia: Saunders; 2014 p. 500.
8. Nakayama T, Toguchida J, Wadayama B, Kanoe H, Kotoura Y, Sasaki MS. MDM2 gene amplification in bone and soft-tissue tumors: association with tumor progression in differentiated adipose-tissue tumors. *Int J Cancer*. 1995;64(5):342–6. [PubMed: 7591308]
9. Mentzel T, Palmedo G, Kuhn C. Well-differentiated spindle cell liposarcoma ('atypical spindle cell lipomatous tumor') does not belong to the spectrum of atypical lipomatous tumor but has a close relationship to spindle cell lipoma: clinicopathologic, immunohistochemical, and molecular analysis of six cases. *Mod Pathol*. 2010;23:729–36. [PubMed: 20228779]
10. Larousserie F, Chen X, Ding Y, et al. Parosteal Osteoliposarcoma: a new bone tumor (from imaging to immunophenotype). *Eur J Radiol*. 2013;82:2149–53. [PubMed: 22178310]
11. Teoh LC, Chan LK, Lai SH. Ossifying lipoma of the hand: a case report. *Ann Acad Med Singap*. 2001;30(5):536–8. [PubMed: 11603142]
12. Weingertner N, Neuville A, Chibon F, Ray-Coguard I, Marcellin L, Ghnassia JP. Myxoid liposarcoma with heterologous components: dedifferentiation or metaplasia? A FISH-documented and CGH-documented case report. *Appl Immunohistochem Mol Morphol*. 2015;23(3):230–5. [PubMed: 25747531]
13. McCormick D, Mentzel T, Beham A, Fletcher CD. Dedifferentiated liposarcoma. Clinicopathologic analysis of 32 cases suggesting a better prognostic subgroup among pleomorphic sarcomas. *Am J Surg Pathol*. 1994;18(12):1213–23. [PubMed: 7977944]
14. Fanburg-Smith JC, Miettinen M. Liposarcoma with meningotheelial-like whorls: a study of 17 cases of a distinctive histological pattern associated with dedifferentiated liposarcoma. *Histopathology*. 1998;33(5):414–24. [PubMed: 9839165]
15. Zajicek AK, Bridge JA, Akers JW, McGarry SV, Walker CW. Dedifferentiated liposarcoma of the lower extremity with low-grade dedifferentiation and low-grade osteosarcomatous component. *Skelet Radiol*. 2017;46:265–71.
16. Kanojia D, Nagata Y, Garg M, et al. Genomic landscape of liposarcoma. *Oncotarget*. 2016;6(40):42429–44.

Fig. 1.

a AP view of a radiograph of the left hand at initial presentation to the outside institution shows a diffusely infiltrating multi-lobulated mass with areas of ossification. The ossification (arrows) is peripheral and curvilinear. **b** Coronal PD MRI of left hand image shows lipomatous lobules (*) containing intermediate signal foci (arrows) corresponding to ossification on the radiograph. The lipomatous lobules blend with adjacent normal fatty tissue. **c** Axial STIR MRI image shows that nodules contain heterogeneously high signal lobules, and given the ossification on the radiograph, these nodules probably represent chondroid elements

Fig. 2.
a Preoperative photograph, volar view. **b** AP view of the radiograph of the left hand at presentation to our hospital shows an increase in size and ossification of the mass

Fig. 3. Left hand mass biopsy **a** Photomicrograph showing atypical lipomatous tumor with adipocytes of varying size and atypical cells with hyperchromatic, irregular nuclei (H&E stain at 200×). **b** Osteocartilaginous metaplasia showing benign bone and cartilage with endochondral ossification, associated with marrow elements (H&E stain at 100×)

Fig. 4.
a FISH showing amplification of MDM2. **b** SNP array analysis showed copy number gain of 3q11.2 and 3q12 and copy number gain of 12q12–12q24.23 with amplification of CDK4 and MDM2 genes confirming the FISH findings. The amplicon on 3q11.2 involved EPHA6 (Ephrin receptor A)

Fig. 5.
Dedifferentiated liposarcoma: Photomicrograph shows cellular spindle cell tumor with mitoses without an adipocytic component (H&E stain at 200×)

Fig. 6.

Imaging studies performed 1 year after staged debulking. **a** AP view of the radiograph shows increased dense central ossification (arrowhead) along the distal third and fourth rays. **b** Coronal T1-weighted MRI and **c** coronal T2-weighted fat-suppressed MRI images reveal that many nodules (*) are non-lipomatous, corresponding to the increased ossification in the radiograph, consistent with dedifferentiated tumor. **d** Post-contrast axial T1-weighted fat-suppressed MRI image of the left arm shows a subcutaneous nodule (arrow) abutting the cephalic vein (arrowhead). **e** Axial CT image shows a round nodule (arrowhead) in the right lung base, suspicious for metastasis. **f** Whole-body MIP image of PET 1 year following staged debulking revealed intense FDG avidity in the left hand mass (large arrow), a right

lung base nodule (arrowhead), left subpectoral adenopathy (small arrow), and left mid arm nodule (curved arrow)

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Fig. 7.

a Dedifferentiation with osteosarcomatous morphology: Photomicrograph showing plump spindle and epithelioid cells with prominent nucleoli incorporating into an immature bony matrix (H&E stain at 200×). **b** Photomicrograph of the non-calcified tumor showing areas retaining an atypical lipomatous tumor morphology consisting of irregular hyperchromatic and focally multinucleated cells in a fibrous stroma with adipocytes (H&E stain at 400×)

Fig. 8.

Follow-up CT of the chest, abdomen, and pelvis 2.5 years following staged debulking. **a** Axial CT chest image reveals an increase in pulmonary metastases. **b** Axial CT abdominal image shows a new pancreatic mass (arrow) and increasing subcutaneous and paraspinal nodules (arrowheads). **c** Axial CT pelvis image shows multiple subcutaneous and muscular nodules (arrowheads) and peritoneal implant (black arrow)