



Case report

When is a lipoma not a lipoma? Case report presenting a lipoblastoma-like tumor of the gluteal cleft in an older gentleman with literature review

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ARTICLE INFO

Keywords:

Case report
Lipoblastoma-like tumor
Lipoblastoma
Lipoma
Male patient
Gluteal cleft

ABSTRACT

Introduction and importance: Lipoblastoma-like tumors are rare tumors that can be confused with lipoblastomas and liposarcomas but have distinct characteristics. This tumor has previously been identified in the vulva of females, and recently in isolated cases of young males. Given its rarity, we present an instance of this tumor in an older man, demonstrating that this pathology is not limited to a specific age or sex, and surgeons and pathologists must be aware of it in their differential.

Case presentation: A 58-year-old male presented for evaluation of an enlarging mass in his right gluteal cleft. Prior to referral for surgical evaluation, the patient underwent an ultrasound-guided biopsy of the mass. Histologically, the tumor was a low-grade cellular spindle cell neoplasm in a fibrous to myxoid stroma. Immunohistochemical and molecular workup ruled out several malignant mesenchymal neoplasms, including myxoid liposarcoma, dedifferentiated liposarcoma, melanoma, low-grade fibromyxoid sarcoma, and sarcomatoid carcinoma. The patient initially declined surgery, but the mass continued to grow, and excision was chosen given the uncertain pathology. The tumor was resected with negative margins and histologically characterized as a “lipoblastoma-like lesion”, with features of a myxoid liposarcoma and spindle cell lipoma. Seven months post-resection, there were no signs of recurrence or metastasis.

Clinical discussion: Despite radiologic and pathologic similarities to malignant lipomatous tumors, lipoblastoma-like tumors are benign and have a good prognosis.

Conclusions: Clinicians should be aware of this entity despite its rarity as resection with negative margins is curative and may be needed to rule out more aggressive tumors.

1. Background

Lipoblastoma-like tumors (LLT) were first described by Lae et al. as benign adipocytic tumors of the female vulva morphologically distinct from lipoblastomas and liposarcomas [1]. Histologically, LLTs are composed of spindle cells in a rich myxoid stroma with prominent vasculature and varying amounts of adipocyte differentiation. They share features of lipoblastomas, myxoid liposarcoma, and spindle cell lipomas [2,3]. In more recent years, the molecular markers of LLTs have

been characterized, displaying differences from these other lipomatous tumors. Molecularly, they are characterized by a lack of PLAG1 and HMGA2 expression, and DDIT3 rearrangement, distinguishing them from lipoblastomas and myxoid liposarcomas respectively [2,4]. However, there is no consensus on the exact molecular profile of LLTs as there have been discrepancies in expression of a variety of molecular markers such as Rb, CD34, and S100. One group reported lack of Rb expression while another reported Rb expression, with intact *RB1* genes [2,4]. There is even less of a consensus on CD34 and S100 expression in

Abbreviations: CDK4, cyclin-dependent kinase 4; CT, computed tomography; DDIT3, DNA Damage Inducible Transcript 3; FISH, fluorescence *in situ* hybridization; FUS, fused-in-sarcoma; HMGA2, High Mobility Group AT-Hook 2; IHC, immunohistochemistry; LLT, lipoblastoma-like tumor; MDM2, mouse double minute-2; MUC4, mucin 4; NTRK, neurotrophic tyrosine receptor kinase; RAF, rapidly accelerated fibrosarcoma; RB/Rb, retinoblastoma; SMA, smooth muscle actin; SOX, Sry-type HMG box.

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<https://doi.org/10.1016/j.ijscr.2022.106889>

Received 8 February 2022; Received in revised form 22 February 2022; Accepted 26 February 2022

Available online 1 March 2022

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LLTs. LLTs have been reported to be CD34⁺S100⁺ [5], S100⁻ and occasionally CD34⁺ [4], and CD34⁻, without reporting S100 expression [1,4–6], making them share similarities with atypical spindle cell lipomatous tumors, atypical pleomorphic lipomatous tumors, and spindle cell tumors, which are all variably CD34⁺S100⁺ [3,7], or myxoid liposarcomas, which are CD34⁻ and variably S100⁺ [8,9]. The difficulty with these molecular discrepancies is that it does not allow diagnostic differentiation between LLTs and other lipomatous tumors such as atypical spindle cell lipomatous tumors, atypical pleomorphic lipomatous tumors, and spindle cell tumors and thus clinicians should be familiar with this entity.

To date, there have been 19 cases of LLT of the vulva [1,2,4,10], and 2 cases of LLTs in young males [5,6]. Our report of an older male who was found to have a LLT adds to this body of literature and demonstrates that these tumors are not predicated on a specific age or sex. A review of the current literature and discussion of this case of LLT is presented.

This case report has been reported in line with the SCARE Criteria [11] and the patient provided verbal consent to report his case.

2. Case presentation

A 58-year-old healthy, independent Caucasian male, with past medical history only significant for a right shoulder lipoma, no history of alcohol/tobacco/drug use, and no family history of cancer, presented to the general surgery clinic at the Malcom Randall Veterans Administration Medical Center with a 4-year history of an asymptomatic, palpable right gluteal mass. The patient previously underwent a core needle biopsy that demonstrated a low-grade spindle cell tumor of the myxoid variety but declined surgical excision. The mass continued to grow over the ensuing two years, and he re-presented to surgical clinic. On physical exam, the gluteal mass was approximately 7 cm, mobile, without overlying skin changes, and located within the intergluteal cleft. Inguinal lymph nodes were non-palpable bilaterally and examination was otherwise unremarkable. Repeat CT scan confirmed an irregular lobulated subcutaneous soft tissue mass that had grown from 5.1 × 1.7 cm (Fig. 1A) to 7.2 × 4.3 cm over the two years (Fig. 1B). The patient subsequently underwent surgical excision by a surgical oncologist with over 15 years of experience, given the growth and worsening discomfort.

On final pathology, a well-circumscribed 5.5 × 5.0 × 4.0 cm mass without a definitive capsule was identified with negative pathologic margins. Histologic evaluation revealed a bland spindle to epithelioid cellular proliferation with only rare “ice cream cone” lipoblast-like cells. The background stroma was collagenous to myxoid stroma with a prominent network of thin, arborizing vessels (Fig. 2). Immunohistochemistry showed diffuse S100 and CD34 staining, intact Rb expression, scattered CDK4 nuclear activity, but no MDM2 IHC reactivity or MDM2

rearrangement by FISH. In addition, there were no demonstrable DDIT3 or FUS rearrangement (characteristic of myxoid liposarcoma [12]) by FISH. Final pathology confirmed a lipoblastoma-like tumor. Surveillance MRI at 4 months and physical exam at 4 and 7 months post-operation demonstrated no evidence of recurrence. Recovery was as expected, with no complications. The patient reports no issues since the procedure, was happy with the outcome, and no further follow-up was required.

3. Discussion

We present the third case of a lipoblastoma-like tumor in a male, and the first in an older male to our knowledge (Table 1). This case report demonstrates that this pathology is not limited to a specific age or sex, and surgeons and pathologists must be aware of it in their differential. LLTs are a rare type of benign myxoid adipocytic tumors that comprise a heterogeneous group of both benign and malignant adipocytic tumors which can have varying amounts of myxoid components [3]. The differential diagnosis includes myxoid liposarcoma, dedifferentiated liposarcoma, atypical spindle cell lipomatous tumor, and low-grade fibromyxoid sarcoma [3,8,13].

When our patient first presented with a soft tissue tumor 2 years prior, ultrasound-guided needle biopsy showed a spindle cell neoplasm in a myxoid stroma, and molecular characterization ruled out major malignant neoplasms, when it was found to be negative for DDIT3 and MDM2 by FISH and had only focal non-specific MUC4 immunostaining. Hence, myxoid liposarcoma, dedifferentiated liposarcoma, and low grade fibromyxoid sarcoma were ruled less likely [8,13,14], which allowed the patient to safely delay resection for two years without any treatment.

Given the findings on imaging, the differential is broad but from a clinical, pathologic, and molecular standpoint, LLTs have similarities to low-grade myxofibrosarcoma (similar morphological appearance, but intact Rb expression and lack of SMA expression argues against this) [15], cellular angiofibroma (similar morphological appearance, both desmin⁻ CD34⁺, but intact Rb and S100 expression argues against this) [14,16], atypical spindle cell lipomatous tumor (both are negative for MDM2 amplification, CD34⁺S100⁺, but Rb is typically lost in this tumor) [7], myxoid liposarcoma (both negative for MDM2 amplification and S100⁺, although the absence of DDIT3 translocation argues against this) [3,9,17], and spindle cell tumors (both SOX10⁻CD34⁺S100⁺, but lacking NTRK expression/gene fusion commonly found in spindle cell tumors makes it unlikely) [18].

Ultimately, a diagnosis of LLT was rendered because it was composed predominantly of spindle cells with rare lipoblastic differentiation and prominent vasculature [2], was negative for DDIT3, FUS, and MDM2 gene rearrangements [2,4,5], negative for STAT6 and MDM2 IHC

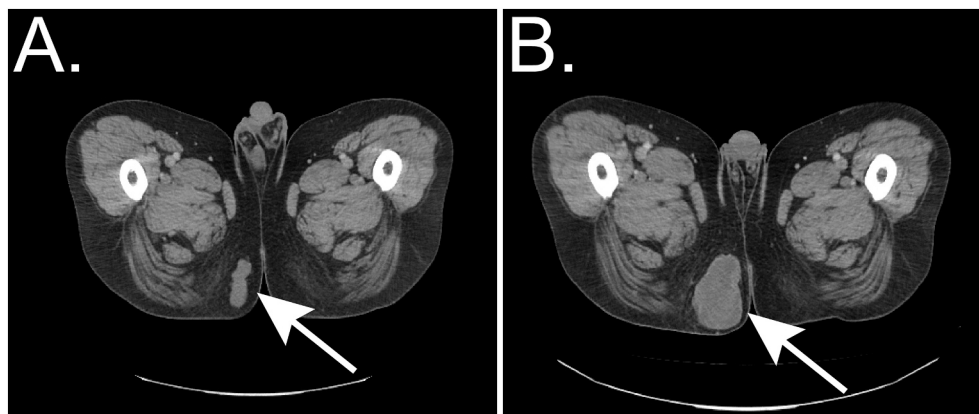


Fig. 1. Axial computed tomography of the described patient at initial presentation (A) and 1.5 years later (B) with an irregular, lobulated mass (arrow) in the subcutaneous tissue of the right gluteus.

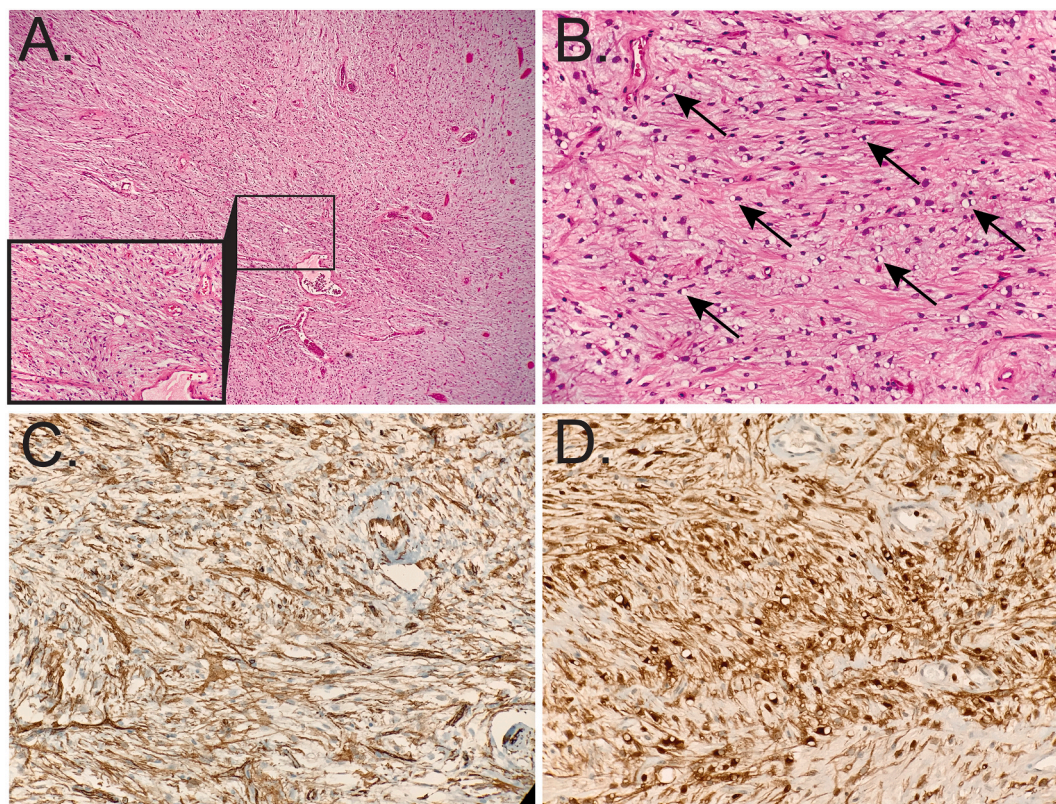


Fig. 2. Photomicrographs of the resected lipoblastoma-like tumor demonstrate mature adipocytes admixed in a sea of spindle cells (A, inset 100× magnification). Lipoblastic differentiation is demonstrated by the enumerable small adipocytes (B, arrows). The tumor was diffusely positive for CD34 (C) and S-100 (D), typical for lipoblastoma-like tumors.

Table 1
Literature summary of lipoblastoma-like tumors.

Year	Study	Cohort size	Sex	Median age (years)	Tumor location	Margin status	Genetic alterations	Protein alterations
2002	Lae [1]	3	Female	23	Vulva	Unknown	Not performed	Negative for CD34, SMA, and desmin expression
2007	Atallah [10]	1	Female	15	Vulva	Unknown	Not performed	Not performed
2015	Mirkovich [4]	8	Female	27	Vulva	Positive (6 of 8)	No <i>DDIT3</i> rearrangement (5 tested)	Loss of Rb expression in 6 out of 7 tumors Negative for S100 (5 tested) Loss of CD34 expression in 2 out of 5 tumors
2018	Schoolmeester [2]	7	Female	35	Vulva	Unknown	No <i>DDIT3</i> or <i>PLAG1</i> rearrangement No <i>RB1</i> regional gain or loss (6 tested)	Weak/mosaic Rb expression
2020	Droop [5]	1	Male	20	Spermatoc cord	Unknown	No <i>MDM2</i> amplification No <i>DDIT3</i> rearrangement No <i>PLAG1</i> , <i>NCOA2</i> , <i>FOXO1</i> alterations	Patchy loss of Rb expression Positive for S100 Focal CD34 expression
2021	Gambarotti [6]	1	Male	17	Spermatoc cord	Unknown	No <i>MDM2</i> amplification No <i>PLAG1</i> , <i>HMG2</i> , <i>EWSR1</i> , <i>FUS</i> alterations	Negative for STAT6, SMA, and desmin Patchy loss of Rb expression Positive for MDM2 expression
2022	Yergin ^a	1	Male	58	Gluteal area	Negative	No <i>MDM2</i> amplification No <i>DDIT3</i> or <i>FUS</i> rearrangement	Negative for CD34 and STAT6 Intact Rb, CD34, and S100 expression Weak MDM2 expression Negative for STAT6, SMA, desmin, SOX10, SMA, NTRK, MUC4

^a Presenting case.

reactivity [5,6], and had intact Rb expression (similar to cases reported by Schoolmeester et al. [2]). Comparing the molecular markers of LLTs reported to date (See Table 1), it appears that in general, LLTs lack *DDIT3* and *PLAG1* translocations, *MDM2* amplification, are variably reactive for CD34, Rb1, and S100, and are non-reactive for STAT6, SMA,

and desmin. Of the 22 reported cases of LLTs, there was no report of distant metastases after a median follow-up of 12.5 months. There were 4 reports of local recurrence, 3 of which had positive surgical margins and 1 that had been treated with “simple or conservative excision” but margins unknown. None of the cases with negative margins had

evidence of recurrence at a median of 7 months after resection.

In conclusion, in the setting of a lipomatous tumor characterized as a myxoid spindle cell neoplasm on biopsy, characterization with the above markers may help to determine if the patient has a lipoblastoma-like tumor rather than a malignant lipomatous tumor regardless of the age or sex of the patient. If the patient is determined to have a lipoblastoma-like tumor or equivocal pathology, surgical excision with negative margins offers curative treatment with a low risk of recurrence.

Provenance and peer review

Not commissioned, externally peer-reviewed, not presented at any conference or regional meeting.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

Institutional Review Board approval was not needed for this single patient case study per institutional policy.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Authors' contributions

Study conception (CGY), pathologic evaluation and pictures (MC), manuscript preparation (CGY, RMT), final manuscript approval (CGY, MC, RMT).

Research registration

N/A.

Guarantor

Ryan M. Thomas, MD.

Declaration of competing interest

The authors declare that they have no competing interests.

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