Title
Irregular Lipomatous Extremity Tumor

Journal
JAMA, 321(17)

ISSN
0098-7484

Authors
Graham, Danielle S
Kadera, Brian E
Eilber, Fritz C

Publication Date
2019-05-07

DOI
10.1001/jama.2019.3719

Peer reviewed

JAMA – Clinical Challenge

Irregular Lipomatous Extremity Tumor

Danielle S. Graham, MD, MBA,[1,2] Brian E. Kadera, MD,[1,2] Fritz C. Eilber, MD[1,2]

1. Division of Surgical Oncology, University of California Los Angeles Medical Center, Los Angeles, CA
2. UCLA - Jonsson Comprehensive Cancer Center Sarcoma Program, University of California Los Angeles Medical Center, Los Angeles, CA

A 71-year-old otherwise healthy female presents with an enlarging, painless mass in her right gluteal area. On exam, she has a large, immobile, non-tender right gluteal mass. She has no neurovascular deficits. CT reveals an 11cm heterogeneous lipomatous tumor involving the right gluteal musculature. What is the differential diagnosis and what would you do next?

Case Scenario

A 71-year-old otherwise healthy female presented with an enlarging, immobile, painless mass in her right gluteal area. She has no other associated symptoms. On exam, she has a large, palpable, non-tender right gluteal mass. She has no neurovascular deficits. Laboratory

studies are within normal limits. CT reveals an 11cm heterogeneous lipomatous tumor involving the right gluteal musculature (Figure 1).

What Would You Do Next?

A. Incisional biopsy of the lesion

B. Core-needle biopsy of the lesion

C. Simple excision of the lesion

D. Repeat imaging in 6 months

Diagnosis: Well-differentiated / de-differentiated liposarcoma

What to Do Next:

B. Core-needle biopsy of the lesion

Core-needle biopsy should be performed to obtain tissue diagnosis. Incisional biopsy should be avoided and can complicate surgical and oncologic management (1). Surgical management should be deferred until a tissue diagnosis is made and pre-operative workup is complete. As this tumor is enlarging, >5cm, deep (sub-fascial), and heterogeneous, it should be considered malignant until proven otherwise. Repeat imaging is unnecessary and inadequate.

Discussion

Liposarcomas are rare, often aggressive, malignancies that require surgical resection and multidisciplinary management. There are approximately 2,400 new cases of liposarcoma diagnosed in the United States per year (2, 3). Subtypes of liposarcoma include well-differentiated, de-differentiated, myxoid, and pleomorphic. Of note, a well-differentiated liposarcoma of the extremity may also be referred to as an atypical lipomatous tumor.

As with all soft tissue sarcomas, liposarcomas are most frequently found on the extremities or in the retroperitoneum. Lipomatous tumors are relatively asymptomatic. A lipomatous tumor arising in the extremity typically presents as a painless mass and in the retroperitoneum occasionally with vague abdominal symptoms.

Cross-sectional imaging, either CT or MRI, should be obtained for all patients. Extremity tumors that are large (>5cm), sub-fascial, or enlarging and any retroperitoneal mass should be considered malignant until proven otherwise. In most cases, core-needle biopsy should be obtained for tissue diagnosis. Incisional biopsy should be avoided and can complicate surgical and oncologic management (1). MDM2 amplification, detected by fluorescence *in situ* hybridization (FISH), can provide additional information. This is particularly useful in distinguishing a well-differentiated liposarcoma (MDM2 amplification)

from a benign lipoma (no MDM2 amplification), as this is often a difficult histologic and/or radiologic distinction (4). De-differentiated (MDM2 amplification), myxoid (no MDM2 amplification), and pleomorphic (no MDM2 amplification) liposarcomas have more characteristic appearances on histology and imaging, so MDM2 amplification may be less useful in these cases.

All patients diagnosed with liposarcoma should undergo CT of the chest to complete pre-operative staging, as sarcomas spread hematogenously, most frequently to the lung. A chest x-ray may be an appropriate substitute for CT of the chest for patients diagnosed with an extremity well-differentiated liposarcoma / atypical lipomatous tumor. Patients diagnosed with myxoid liposarcoma should additionally undergo CT of the abdomen/pelvis and be considered for MRI spine, as this liposarcoma subtype can metastasize to other anatomic locations.

Surgery remains the mainstay of treatment for liposarcoma and oncologic margin-negative resection is associated with improved disease-free survival. Amputation is rarely, if ever, required for primary extremity disease. Identifying malignant tumors pre-operatively is critical for surgical planning and avoiding unnecessarily morbid operations to obtain local control. A patient that undergoes a simple excision for a presumed lipoma that is found to be a liposarcoma should undergo repeat imaging and often a wide re-resection of the

surgical site as there is a 50-80% rate of gross residual disease in this setting (5).

Radiation therapy has been shown to improve local control for patients with primary high-grade extremity soft tissue sarcomas, including liposarcomas. However, the exceptions of the use of radiation are small, low-grade liposarcomas or well-differentiated liposarcomas / atypical lipomatous tumors, given their low risk of recurrence and the potential long-term complications from radiation (6). Although the benefit is less clear for retroperitoneal disease, radiation may be used in highly selected cases for the treatment of aggressive histologic subtypes by centers with expertise in treating sarcoma in this location. For both the extremity and retroperitoneum, pre-operative (neoadjuvant) radiation is preferred due to its favorable late toxicity profile, shorter course, and potential operative benefits of downsizing the tumor (7). The benefit of systemic therapy (chemotherapy, molecularly-targeted therapy, or immunotherapy) for high-risk liposarcomas is less clear and is only considered for specific histologic subtypes or for patients with metastatic or locally advanced disease (8).

Risk of local recurrence (5% to 15%) and distant metastasis (5% to 70%) of extremity liposarcomas ranges widely and is dependent on the histologic subtype, grade and size. In comparison to extremity liposarcomas, the risk of local recurrence for retroperitoneal

liposarcomas is significantly higher (40% to 50%). Widely-validated prognostic models or nomograms more accurately determine oncologic prognosis than existing TNM staging systems. Websites, such as the MSKCC nomogram, and applications, such as Sarculator (which uses validated nomogram data), give patient-specific prognosis data and are utilized by sarcoma oncologists and patients alike (9).

A patient that is diagnosed with liposarcoma should be referred to a sarcoma specialty center whenever possible, as multidisciplinary treatment and surveillance by physicians specializing in sarcoma has been shown to improve patient outcomes (10).

Patient Outcome

Core-needle biopsy revealed a spindle and pleomorphic sarcoma, most consistent with a well-differentiated / de-differentiated liposarcoma with MDM2 amplification present. CT of the chest showed no systemic disease. After a multidisciplinary discussion, the patient underwent neoadjuvant radiation followed by resection. She has undergone surveillance imaging every 6 months since her surgery and remains disease free two years post-operatively.

Article Information

Corresponding Author: Fritz C. Eilber, MD, Division of Surgical Oncology, University of California Los Angeles, 10833 Le Conte Ave, 54-140 CHS, Los Angeles, CA 90095 (fceilber@mednet.ucla.edu).

Conflict of Interest Disclosures: Dr. Graham and Dr. Kadera have no disclosures. Dr. Eilber is a member of the Scientific Advisory Board of Certis Oncology.

Additional Contributions: We thank the patient for providing permission to share his information.

References

1. Wilkinson MJ, Martin JL, Khan AA. Percutaneous core needle biopsy in retroperitoneal sarcomas does not influence local recurrence or overall survival. *Ann Surg Oncol*. 2015;22(3):853-8.
2. PDQ® Adult Treatment Editorial Board. PDQ Adult Soft Tissue Sarcoma Treatment. Bethesda, MD: National Cancer Institute. Updated 01/29/2019. Available at: https://www.cancer.gov/types/soft-tissue-sarcoma/hp/adult-soft-tissue-treatment-pdq. Accessed 03/11/2019. [PMID: 26389481]
3. Brennan MF, Antonescu CR, Moraco N. Lessons learned from the study of 10,000 patients with soft tissue sarcoma. *Ann Surg*. 2014;260(3):416-21.

4. Clay MR, Martinez AP, Weiss SW, Edgar MA. MDM2 Amplification in Problematic Lipomatous Tumors: Analysis of FISH Testing Criteria. *Am J Surg Pathol*. 2015;38(10):1433-9.
5. Taub F, Griffin AM, Wunder JS, Ferguson PC. Influence of unplanned excision on the outcomes of patients with stage III extremity soft-tissue sarcoma. *Cancer*. 2018;124(19):3868-3875.
6. Sommerville SM, Patton JT, Luscombe JC, Mangham DC, Grimer RJ. Clinical outcomes of deep atypical lipomas (well-differentiated lipoma-like liposaromca) of the extremities. *ANZ J Surg*. 2005;75(9):803-6.
7. O'Sullivan B, Davis AM, Turcotte, R, et al. Preoperative versus postoperative radiotherapy in soft-tissue sarcoma of the limbs: a randomized trial. *Lancet*. 2002;359(9325):2235-41.
8. Woll PJ, Reichardt P, Cesne AL, et al. Adjuvant chemotherapy with doxorubicin, ifosfamide, and lenograstim for resected soft-tissue sarcoma (EORTC 62931): a multicenter randomised controlled trial. *Lancet*. 2012;13(10):1045-1054.
9. Eilber FC, Brennan MF, Eilber FR, Dry SM, Singer S, Kattan MW. Validation of postoperative nomogram for 12-year sarcoma-specific mortality. *Cancer*. 2004;101(10):2270-5.
10. Gutierrez JC, Perez EA, Moffat FL, Livingstone AS, Franceschi D, Koniaris LG. Should soft tissue sarcomas be treated at high-volume

centers? An analysis of 4205 patients. *Ann of Surg*. 2007;245(6):952-958.

Figures

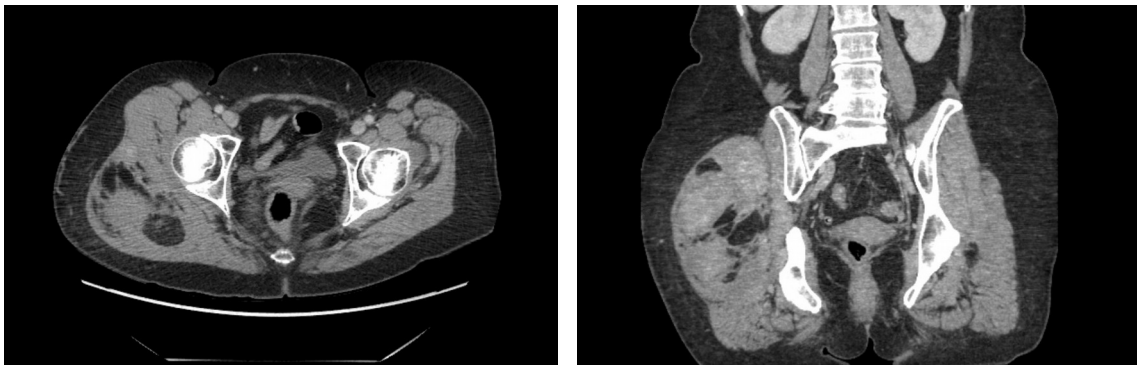

Figure 1: Axial and coronal CT of a large, heterogeneously enhancing right gluteal mass.