CLINICAL VIGNETTE

Atypical Lipomatous Tumor

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Case Report

A 65-year-old female presented to medical oncology for an evaluation of recently diagnosed atypical lipomatous tumor of the left buttock. Her past medical history included pre-hypertension, pre-diabetes, dyslipidemia, actinic keratosis, and resected stage 0 melanoma. She initially noted a small lump on her left buttock approximately three years prior. The lump slowly grew, eventually leading to mild pain and discomfort upon seating. When her primary care doctor evaluated her, the mass was approximately 20 cm by 16 cm. An MRI pelvis with/without contrast revealed a large non-enhancing lipomatous lesion in the left gluteal musculature which, favored to represent a lipoma. She underwent an excision of the left buttock subfascial mass by a general surgeon. A large mass measuring 16 x 10 x 5 cm was excised along with two additional smaller lipomatous lesions superiorly, which were both approximately 2 cm in size. The pathology from three tumors were atypical lipomatous tumors/well-differentiated liposarcomas - histologic grade 1 with 0 mitoses per 10 high power fields (HPF). The surgical margins could not be assessed, and the final pathologic stage was pT3NxMx, stage 1B. The concurrent FISH test was positive for *MDM2* amplification.

Discussion

Atypical lipomatous tumor (ALT) is a mesenchymal neoplasm composed of adipocytic proliferation with multiple morphologic subtypes and significant histologic variability.[1,2] It is the most common adipocytic malignancy (40-45% of all liposarcomas) and most commonly found in adults between 50 to 60 years old. The incidence is reported as 1/200,000 per year[3,4] and some use ALT to describe deep-seated lesions and WDL for more superficial lesions. Others refer to ALT as WDL arising on the trunk and extremities. They are genetically and morphologically the same.[2,4] ALT is also known as well-differentiated liposarcoma (WDL). There is currently some controversy about terminology.

ALT is considered an 'intermediate' type of adipocytic tumor. It is locally aggressive with low metastatic potential.[5] The most common site of ALT is the deep tissue of the proximal extremities (buttock and thigh), followed by the retroperitoneum, trunk, head and neck, and spermatic cord.[1,2,4] Tumors in the extremities have very low metastatic potential, but deep-seated tumors can dedifferentiate and metastasize.

ALT can be firm or soft and fleshy. Grossly it is typically large, well-circumscribed, and multilobulated. Microscopically, it is generally composed of mature fat with different-sized adipocytes and bands of fibrotic stroma with spindle cells with enlarged, hyperchromatic nuclei.

Atypical cells are frequently located in the fibrous areas. Some lipoblasts may be found but are not required for diagnosis. It also has extensive chromosomal aberrations, and 90% of cases include amplification of the chromosomal region 12q13-15.[3] This leads to overexpression of *MDM2* (murine double minute 2) and *CDK4* (cyclin-dependent kinase 4). Abnormal FISH or PCR of *MDM2* and/or *CKD4* can distinguish ALT from benign adipose tumors such as lipoma.[6,7.]

Typically once a soft tissue mass is noted, an ultrasound, CT, or MRI of the affected body part is performed. Extremity lesions are sometimes surgically removed without biopsy. Deeper lesions may prompt percutaneous biopsy if the surgical resection is morbid. Frequently the diagnosis of ALT is frequently only confirmed after surgical excision of the mass. Many are initially thought to be benign lipomas.

The mainstay treatment for an ALT is surgical resection. Complete resection of the tumor in the extremities and truck is typically feasible and can be curative. If the surgical margin is negative, no further therapy is recommended. ALTs in the retroperitoneum and inguinal areas are more difficult to completely resect. They tend to recur more and have higher likelihood to dedifferentiate and metastasize. Extended resection involving en-bloc removal of adjacent uninvolved organs and structures, when feasible, may decrease local recurrence rates.[8] Adjuvant radiation therapy is also a controversial potential treatment. Radiation therapy reduces local recurrence rate, especially for R1 or R2 resection tumors, but does not improve overall survival. Many local recurrences can be treated with re-operation, and adjuvant radiation therapy could be deferred for patients with extremities tumors where re-operation is feasible. Adjuvant radiation therapy would be considered for tumors involving vital structures with complicated re-operation.[9] Chemotherapy currently has a minimal role in treating ALT. It is typically reserved for patients with advanced, unresectable ALT and dedifferentiated liposarcoma (DDLS). Anthracycline-based chemotherapy is the first-line systemic treatment. However, it has not led to good clinical outcomes. Single-agent anthracycline has a low objective response rate of

around 12%. Adding alkylating agent ifosfamide increases the response rate to 26% but does not improve overall survival.[7,10] Because overexpression of *CDK4* is common in ALT and DDLS, *CDK4* inhibitor palbociclib has been studied in this group and reports progression-free survival (PFS) of 57.2% at 12 weeks and occasional tumor response. One patient in a small study of sixty patients achieved a complete response.[11] Immunotherapy is one of the exciting novel therapeutic options in cancer treatment. Studies report some liposarcomas also have PDL-1.[12,13] A non-randomized, open-label, phase 2 study has shown that PD-1 inhibitor pembrolizumab has meaningful clinical activity in DDLS, with some patients having an objective partial response to treatment.[14]

Clinical Case Follow-up

Because the initial surgical margin could not be assessed, a restaging MRI pelvis revealed two residual focal non-enhancing fatty lobules in the post-surgical bed. These two masses measured 2.5 cm by 1.6 cm and 5.1 cm by 1.2 cm. She was referred to a surgical oncologist because surgical re-resection is the mainstay of treatment and underwent radical resection of the two residual ALTs without complication. She is now being monitored for local recurrence with serial examinations including MRI pelvis every six months.

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