CASE REPORT

From Hemorrhage to Metastasis: A Complex Case of De-differentiated Liposarcoma

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ABSTRACT

Soft tissue sarcomas arise from the body's connective tissues and approximately 50% occur in the extremities. Though these malignancies are rare, they are quite aggressive and can easily metastasize to distant parts of the body, especially the lungs. One subset of sarcomas are liposarcomas which are genetically characterized by the amplification of the MDM2 and CDK4 genes. Surgery is typically the gold standard for localized tumors, however systemic manifestations remain a challenge to treat and require a multidisciplinary approach for effective treatment. We describe a case of a patient who presents with a large de-differentiated liposarcoma of the left lower extremity that is bleeding uncontrollably and found to have metastasized. This report aims to bring attention to a unique presentation of this neoplasm and increase awareness of how quickly these neoplasms can metastasize.

INTRODUCTION

Soft tissue sarcomas are a diverse group of malignancies that occur in the body's connective tissues. Approximately 50% to 60% of sarcomas occur in the extremities, and despite their rarity, they are aggressive neoplasms that often result in death.[1-2] These tumors can become quite large but are usually painless or rarely painful soft-tissue masses. These malignancies occur in approximately one to two individuals per 100,000 worldwide, and about 8,000 new cases occur yearly in the United States.[3] One subgroup of soft tissue sarcomas are de-differentiated liposarcomas (DDL); these neoplasms are high-grade nonlipogenic sarcomas that arise in a background of a preexisting well-differentiated liposarcoma.[4] They are aggressive neoplasms with a metastatic rate of 15-30% and overall mortality rate of 28%.[5] We present an interesting case of a man with a high-grade dedifferentiated liposarcoma to demonstrate the aggressive nature of this neoplasm and highlight the

importance of early intervention for achieving the best outcomes.

CASE PRESENTATION

This is a case of a 42-year-old male with a past medical history of hypertension and left thigh high-grade sarcoma with de-differentiated liposarcoma who presented to the Saint Louis University (SLU) emergency department (ED) due to new onset bleeding from his left thigh mass that began earlier today. The patient has frequently had small amounts of blood and secretions from the mass. However, today, he was unable to control the bleeding, and thus, called Emergency Medical Services (EMS). EMS controlled the bleeding with gauze and bandages, and upon arrival at the hospital, the patient was hemodynamically stable with initial hemoglobin of 12.7. Physical exam was remarkable for a large fungating, necrotic tumor (Figure 1) on the medial aspect of the left thigh, covered in bandages**,** and mild pain to palpation of the left thigh. Motor and sensation of the left distal extremity, as well as 2+ dorsalis pedis and posterior tibial pulses were intact. CT Angiogram of the left lower extremity was also ordered and demonstrated "interval increase in size of the hypervascular mass arising from the medial left thigh compatible with known liposarcoma. No major bleeding vessels identified."

The left thigh mass was first noted six months-one year ago and the patient had been following with an oncologist closer to his hometown. Biopsy of the mass upon initial diagnosis demonstrated a high-grade sarcoma with murine double minute 2 (MDM2) amplification, with dedifferentiated liposarcoma Stage IV. Thus, he was referred to SLU Hospital and had an operation for mass resection scheduled with SLU orthopedic oncology and plastic and reconstructive surgery (PRS) for surgical resection of the mass and left lower extremity reconstruction with possible free vs. locoregional flap the following week. Although his bleeding had stopped, the patient was admitted to internal medicine for assistance with hemostasis and observation prior to his planned operative intervention next week. Initial CT chest/abdomen/pelvis (C/A/P) done at the time of mass discovery showed no metastasis to his chest or abdomen and MRI of his left lower extremity was also notable for nothing other than the mass. Repeat CT C/A/P was ordered upon this admission for definitive staging and demonstrated "interval development of numerous bilateral



Figure 1: Presentation of patient's mass on the medial left thigh from different angles. Tumor appears to be very vascular in nature and pictures were taken after initial bleeding was stopped.

pulmonary nodules suspicious for metastatic disease, largest in the right middle lobe measuring up to 1.3 cm and left upper lobe measuring up to 2 cm." Interventional radiology (IR) was consulted for biopsy of these nodules.

The following day, the patient's serous drainage converted to seropurulent, and he spiked a fever of 102.9ºF and tachycardia up to 110. He had leukocytosis of $13.7x10^9$/L and blood cultures grew *enterococcus faecalis*. PRS was consulted due to concern for superimposed infection of the mass, and he was started on vancomycin and ampicillin. Blood cultures two days later showed no growth, so the original plan to proceed with operative mass removal was continued. The soft tissue sarcoma was removed in its entirety with vacuum-assisted closure of the wound and plan for follow-up in ten days for split thickness skin graft. Follow up with IR for CT guided needle core biopsy of the pulmonary nodules resulted in metastatic sarcoma, consistent with origin from primary thigh dedifferentiated liposarcoma. The patient was then discharged with outpatient oncology follow-up, education on wound vacuum management, and instructions to return for further operative intervention by PRS.

DISCUSSION

Accurate diagnosis of de-differentiated liposarcomas relies on identifying their distinctive chromosomal abnormalities and metastatic profiles. Characterizing these DDLs are specific giant marker chromosomes and a supernumerary ring, both of which contain amplified sequences of 12q13-15 including murine double minute 2 (MDM2) and cyclin-dependent kinase 4 (CDK4) cell cycle oncogenes.[5] Detection of these oncogenes is vital as these serve to distinguish de-differentiated liposarcomas from undifferentiated sarcomas. Given that DDLs are aggressive neoplasms, it is important to check for metastases to other places in the body as well, as was demonstrated by the CT C/A/P in this patient. One retrospective study analyzing data from 148 patients demonstrated that the lung is the most frequent site of metastasis of de-differentiated liposarcomas.[6] They found that the risk of developing metastatic disease was statistically associated with local recurrence and tumor grade.[6-7]

For de-differentiated liposarcomas that occur in the extremities, surgery is the standard treatment and only potentially curative option, regardless of whether there is supplementation by radiotherapy.[4,5,8] Research has shown that the optimal surgical strategy involves complete resection during the initial operation, as was planned for this patient's treatment. A multidisciplinary approach is often recommended in effectively treating this disease, including surgical, medical, and radiation oncology.[7] The treatment for advanced disease manifestations and systemic spread is challenging; however, anthracycline based regimens in combination with alkylating agents are the gold standard for first-line treatment.[9,10] Given the complexity of available therapies, potential toxicities, and the often limited curative options in advanced disease, shared decision-making is essential. This approach fosters collaboration between patients and the multidisciplinary care team, ensuring that therapeutic choices are aligned with the patient's values, goals of care, and quality-of-life considerations.[11] In this patient's case, we had all of these teams on board and had him scheduled for adjuvant radiation therapy with outpatient oncology following resection of his mass. It is important to be aware of how aggressive sarcomas, and more specifically de-differentiated liposarcomas, can be in order to treat patients effectively. Being vigilant about timely CT scans to check for

metastases is vital to detect and treat early when the chance of survival is greatest.

Notes

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