

Iatrogenic Metastasis of Soft-tissue Sarcoma at the Donor Flap Site: Case Report and Proposed Surgical Oncologic Techniques

Christa L. LiBrizzi, MD

Sandesh S. Rao, MD

Sami H. Tuffaha, MD

Adam S. Levin, MD

John M. Gross, MD, MS

Carol D. Morris, MD, MS 

ABSTRACT

An 81-year-old woman with multiply recurrent undifferentiated pleomorphic sarcoma of the foot underwent wide excision and reconstruction with an anterolateral thigh free flap. Six years postoperatively, she developed biopsy-proven recurrence within the harvest site. No other sites of disease were detected on staging workup. The flap site recurrence was attributed to iatrogenic implantation at the time of harvesting.

Iatrogenic metastases are thought to be caused by tumor implantation, which may be attributable to cross-contamination from instrumentation and surgical techniques. In the present article, we highlight preventive techniques and oncologic surgical principles intended to reduce the likelihood of iatrogenic metastasis. Increased awareness by all members of the surgical team may prevent this unfortunate complication.

Soft-tissue sarcomas are rare neoplasms of mesenchymal origin with an age-adjusted incidence of approximately 1% of all adult cancers.¹ The cornerstone of treatment is wide surgical excision. Primary predictors of long-term mortality in soft-tissue sarcomas include local recurrence and development of metastases.^{2,3} Risk of distant metastasis has been associated with large (>5 cm), deep, high-grade tumors.⁴⁻⁶

Iatrogenic tumors are those that have implanted secondary to the manipulation of a tumor during diagnosis or treatment. Regional iatrogenic seeding of tumor cells can occur in the setting of a positive surgical margin, a hematoma, or as a result of the biopsy approach or drain placement.⁷⁻¹¹ Iatrogenic metastases occur at sites remote from the primary tumor because of cross-contamination from instruments or surgical technique.¹²⁻¹⁴ Examples of scenarios in which iatrogenic metastases can occur include secondary exposed surgical sites, as would be created in the setting of free soft-tissue flaps, vascular graft harvest, bone graft harvest, or additional surgical procedures in the same surgical setting.¹⁵⁻²⁰

Here, we describe a case of iatrogenic metastases in extremity reconstruction after sarcoma excision. The patient presented with a high-grade undifferentiated pleomorphic sarcoma (UPS) within the anterolateral thigh (ALT) free flap donor site 2 years after wide excision and coverage of a right dorsal foot UPS. We also propose common surgical oncology techniques, which are taught during orthopaedic surgery fellowship but not widely published, for preventing this

From the Division of Orthopaedic Oncology (Dr. LiBrizzi, Dr. Rao, Dr. Levin, and Dr. Morris), Department of Orthopaedic Surgery, Department of Plastic and Reconstructive Surgery (Dr. Tuffaha), and the Department of Pathology (Dr. Gross), The Johns Hopkins University School of Medicine, Baltimore MD.

Correspondence to Dr. Morris: cmorri61@jhmi.edu

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uncommon complication. The patient was informed that data regarding their case would be submitted for publication, and she provided consent.

Case Report

An 81-year-old woman with a history of biopsy-proven UPS of the dorsal right foot who had undergone successful wide excision and reconstruction with a free flap 6 years earlier presented with a nodule within her ALT flap harvest site. Her surgical history was remarkable for an initial attempt at resection resulting in a positive margin. Repeat excision created a 10 × 12 cm defect with exposed extensor hallucis longus and tibialis anterior on the dorsum of the foot, which was provisionally closed until confirmation of negative margins on permanent pathology, which occurred 1 to 2 weeks after the index surgery. The defect was then covered with an ipsilateral ALT flap.

At the time of the procedure, the subcutaneous tissue, muscle, and tendons of the dorsal foot were first débrided. The dorsalis pedis artery and vein were prepared as recipient vessels. The ipsilateral cutaneous ALT flap was then raised in standard fashion and transferred to the foot. The microvascular anastomoses were uncomplicated, and the flap showed adequate perfusion. The flap donor site was closed with a keystone-type flap from the medial thigh. After débridement of the previous tumor site, there was no documentation of a change of outer gloves or instruments, no change of equipment sets for the thigh versus the foot, and no redraping.

Two years later, the patient had local recurrence, which was widely excised with local reconstruction. Four years later, the patient noticed a dime-sized, firm mass on her anterior thigh near the ALT flap harvest site, which was demonstrated on MRI (Figure 1). An excisional biopsy determined an intermediate-grade UPS (Figure 2) with positive margins. The patient subsequently presented for surgical treatment. She was taken to the operating room for wide excision of the right ALT mass. The previous 5-cm skin incision was elliptically excised with a 2-cm cuff in all directions. The fascia was incised along the ellipse. The specimen was removed en bloc and measured 10 × 4 cm, including margins of deep fascia and muscle. All contaminated instruments were removed from the surgical field. All members of the new surgical team used clean instruments, gloves, and gowns for wound closure. The wound was closed primarily. The patient has since been disease free for 28 months on subsequent surveillance examinations and at no point received neoadjuvant or adjuvant chemotherapy or radiation therapy.

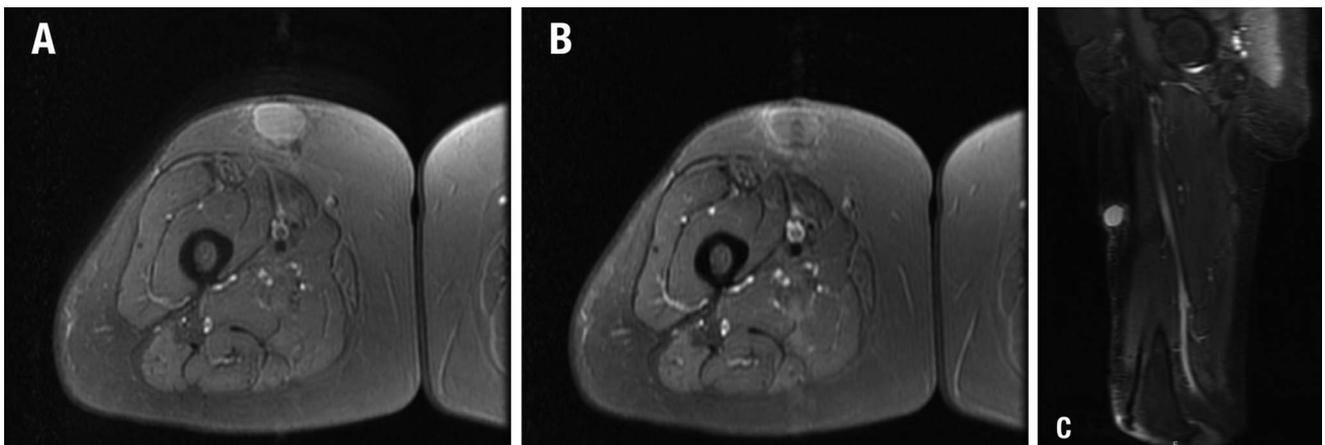
Discussion

Herein, we present a patient with a foot sarcoma who had subsequent recurrence in her ALT flap harvest site, concerning for iatrogenic metastasis thought to be secondary to direct seeding of tumor cells. We are unable to determine whether this was a recurrence or iatrogenic metastasis. A metachronous metastasis is unlikely because of the distant location spanning two joints, the tumor being within the ALT harvest bed, and the patient having been otherwise free of metastatic disease for 6 years. This case highlights the importance of adhering to strict surgical oncology principles.

Cases of iatrogenic metastasis are typically local recurrence within or near the incision or biopsy site. Examples include sarcomas arising in arthroscopic or thoracoscopic port sites.^{17,21} Rarely, distant metastases at bone graft harvest sites have been reported.¹⁶ Cole et al¹⁵ described an osteosarcoma at the harvest site of an iliac crest bone graft obtained for a presumed benign tibial lesion. Direct inoculation of tumor cells at a distant site likely led to tumorigenesis at the distant site. Pichardo et al²⁰ described a patient with squamous cell carcinoma of the hard palate whose excision necessitated a radial forearm free flap reconstruction. Six months postoperatively, the patient presented with iatrogenic metastasis at the free flap harvest site. The authors suspected that cross-contamination may have occurred from bone saw particulate, irrigation spray, and/or surgeons interchanging between the two surgical fields, regardless of the use of separate fields and instrument sets. These cases highlight the importance of meticulous surgical oncology techniques to prevent contamination of adjacent and distant surgical sites and the need for education regarding these techniques.

We hypothesize that iatrogenic metastasis in our patient was caused by surgical cross-contamination of the instruments used in débridement and preparation of the right dorsal foot wound to prepare and transfer the ALT flap. It was not documented whether the surgeons changed gloves after handling the right dorsal foot wound before flap preparation. Although the surgical margins were noted to be negative on the final pathology report after the re-excision, undetected foci of residual disease may have existed.

Fellowship-trained orthopaedic oncologists are rigorously taught surgical oncology surgical protocols and techniques in an effort to avoid contamination, which are taught during fellowship training.²² To our knowledge, no evidence-based resource exists describing safe practices in oncologic reconstruction or effectiveness of these techniques. Below we present the techniques used by the orthopaedic oncology team at our institution. These principles and techniques are used regardless of whether the tumor is

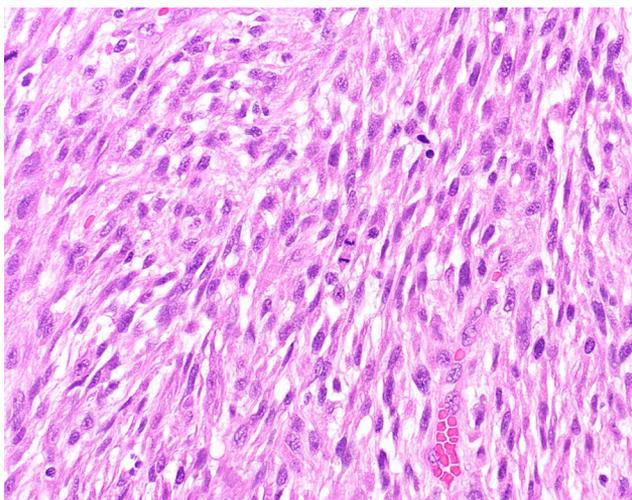
Figure 1

(A) Axial T1 fat-suppressed MRI, (B) axial T1 fat-suppressed MRI with gadolinium contrast, and (C) sagittal short tau inversion recovery imaging demonstrating a $2.1 \times 2.1 \times 2.4$ cm lesion suprafascial to the anterior compartment of the thigh that is T1 and short tau inversion recovery hyperintense to muscle with internal enhancement with gadolinium administration.

thought to be malignant in an effort to prevent tumor contamination.

Authors' Suggested Surgical Oncologic Techniques to Prevent Iatrogenic Metastases

1. Procedures involving multiple surgical sites are avoided when possible. When multiple surgical sites are required during the same surgical case, the non-tumor-contaminated site is draped separately and covered while working on the tumor-

Figure 2

Intermediate-power photomicrograph ($\times 100$ magnification) of pathology specimen from hematoxylin and eosin staining of the nodule near the anterolateral thigh donor site demonstrating spindle cells with nuclear pleomorphism, consistent with the patient's history of undifferentiated pleomorphic sarcoma.

contaminated site. If this precaution is unfeasible (eg, as in a distal thigh sarcoma with popliteus vessel invasion, necessitating vascular repair with an ipsilateral saphenous vein graft), the non-contaminated harvest site is reprepared and draped.

2. If the procedure requires the use of a tourniquet, the limb is exsanguinated via gravity, rather than using an Esmarch bandage, to prevent tumor capsule rupture or intravascular pressurization of tumor cells.
3. All surgical instruments used in the exposure, handling, and delivery of the tumor are considered contaminated. These instruments are placed inside a basin separate from the other surgical instruments. All handles are faced in the same direction to avoid tumor contamination onto handles in the event the instruments need to be reused within the same field.
4. Strict hemostasis is obtained to avoid hematoma formation and a subsequent area of extended contamination. Hemostatic agents are used generously when required.
5. After delivery of the tumor, surgical gloves are changed. Any surgical gowns that are majorly soiled are also changed.
6. After delivery of the tumor, the previously used surgical instruments are not reused. If multiple surgical teams are performing subsequent portions of the procedure, a separate instrument table is prepared away from the surgical field for them.
7. Drains are placed along the longitudinal incision and as close to the edge of the incision as possible to minimize remote contamination. Drain sites

are considered to be potentially contaminated in the setting of biopsies or excisions with unknown margins.

8. The use of a negative pressure wound therapy dressing (wound vacuum-assisted closure) is controversial in wounds of patients with active malignancy. It is possible that tumorigenesis is increased with negative pressure wound therapy as a result of increased angiogenesis and inflammatory pathway modulations leading to a more fertile environment.²³ Recent data suggests no increased risk of recurrence using wounds vacs as a temporizing measure pending final margin review. (Fourman MS, Ramsey DC, Newman ET, Schwab JH, Chen YL, Hung YP, Chebib I, Deshpande V, Nielsen GP, DeLaney TF, Mullen JT, Raskin KA, Lozano Calderón SA. Assessing the Safety and Utility of Wound VAC Temporization of the Sarcoma or Benign Aggressive Tumor Bed Until Final Margins Are Achieved. *Ann Surg Oncol*. 2021 Nov 9. doi: 10.1245/s10434-021-11023-9. Epub ahead of print. PMID: 34751874.)

Our report is limited to just one case, described retrospectively. We are aware of no large multicenter studies documenting the prevalence of particular orthopaedic oncology techniques or outcomes of such cases, which would enable us to put our case in context. Such studies would be difficult to perform because surgical techniques and standards of care vary, leading to numerous confounders; moreover, ethical standards would preclude assigning patients to a control group in which oncological principles are not followed.

Conclusions

Metastasis of both benign and malignant tumors can increase the risks of morbidity and death. Iatrogenic metastasis is a potentially preventable complication. We described a patient with a sarcoma of the right dorsal foot who presented with iatrogenic metastasis within her ALT flap harvest site. Strict adherence to the surgical oncology principles and techniques described herein may decrease the risk of iatrogenic metastases.

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