Tips and Tricks: Vascularized Free Fibula Intercalated Graft for Humeral Shaft Reconstruction after Ewing's Sarcoma Resection

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Introduction

Ewing's sarcoma (EWS) is a small round cell sarcoma which most commonly presents in the metaphysis and diaphysis of long bones, usually with a large associated soft tissue component[1]. It is the second most common primary malignant bone tumor in children after osteosarcoma. EWS is classically defined by a translocation of chromosomes 11 and 22 resulting in the EWSR1-FLI1 fusion protein that acts as an oncogenic transcription factor[2].

The most important prognostic indicator is the presence of metastases at the time of presentation. Twenty five percent of patients present with metastatic disease. Bone or bone marrow metastases portend a worse prognosis than pulmonary metastases. Ten year survival is approximately 60% for localized disease and 30% for metastatic disease[1]. Other negative features include response to chemotherapy, size greater than 8 cm, location and expression of specific genetic markers including p53, Ki-67, or HER-2/neu. The cornerstone of treatment is chemotherapy for systemic control and local control via surgical resection and/or radiotherapy.

The surgical treatment can be done with limb salvage or amputation.Among the alternatives for limb salvage are resection followed by biological reconstruction or endoprosthetic device. Here we report on the use of a vascularized free fibular autograft for humeral reconstruction following resection of a diaphyseal Ewing's sarcoma.

Case Report

History

The patient is a healthy 19 year old male who sustained a left humerus fracture while catching a lightweight object. He reported two months of antecedent humeral pain without constitutional symptoms or prior injury. Imaging obtained at the time of injury demonstrated a pathologic fracture through an aggressive appearing bone lesion at the left midshaft humerus.

Examination

On exam, he had tenderness and swelling around the fracture site. Motor and sensory function was normal in all nerve distributions in the left upper extremity. There was no palpable mass or skin lesions.

Imaging

X-rays of the left humerus were obtained at the time of injury and were notable for a nondisplaced pathologic fracture through a poorly defined, permeative, lytic lesion in the mid-humeral diaphysis (Figure 1). Subsequent contrast enhanced MRI of the humerus was obtained and demonstrated a 5.6 cm x 2.0 cm heterogenous enhancing lesion in the mid-diaphysis with periosteal reaction and a small soft tissue component (Figure 2.).

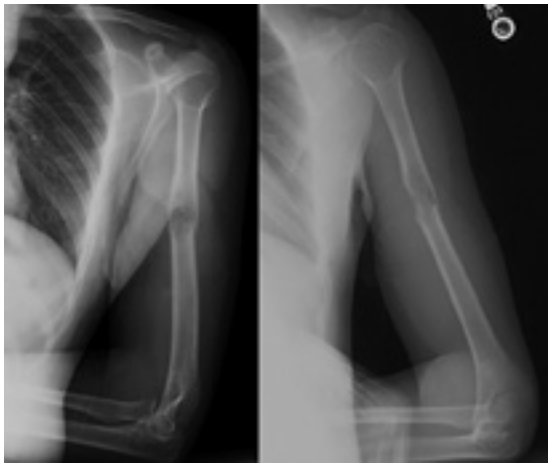

Figure 1. Injury films demonstrating pathologic fracture through lytic lesion in left humeral diaphysis.

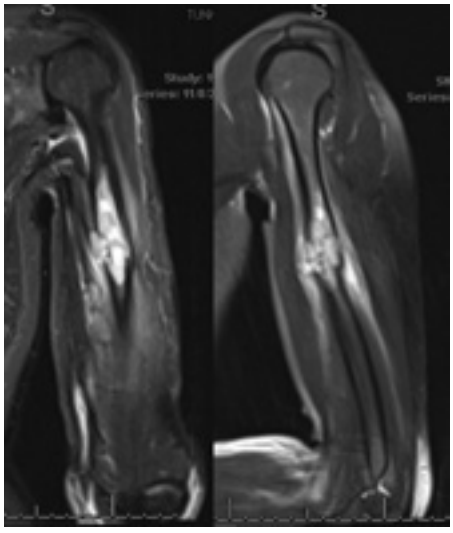

Figure 2. Coronal and sagittal T2 MRI sequences with expansile intramedullary lesion and small soft tissue component.

Management

Given the concern for a malignant process, the decision was made to proceed with a core needle biopsy with Interventional Radiology. Pathology was consistent with a small round cell tumor and RNA sequencing demonstrated EWSR1-NFATC2 fusion protein. The patient underwent the standard work-up including PET scan, CT chest, and bone marrow biopsy, which were negative for metastatic disease. Six cycles of chemotherapy alternating vincristine, Cytoxan, and doxorubicin with ifosfamide and etoposide were administered preoperatively.

Surgical Resection

After completing neo adjuvant chemotherapy, the patient was deemed to be a good candidate for limb salvage with resection of the left humeral Ewing's sarcoma with primary reconstruction with vascularized fibular autograft. This was the ideal approach because imaging suggested that wide resection was possible despite the previous pathologic fracture and that all major neurovascular structures could be spared. The tumor's size was also suitable for reconstruction with fibular autograft.

An extensile approach to the anterior left humerus was used following the deltopectoral interval. The pectoralis major, conjoined tendon, and latissimus dorsi were released and the brachial plexus was identified. The anterior humeral circumflex vessels were ligated (Figure 3A). Distally, the biceps was mobilized and brachialis transected at the predicted resection level. The radial nerve was dissected away from the tumor, the deltoid and triceps were released, and the proximal bone cut was made. After distal dissection of tumor was completed, the distal bone cut was made and the tumor was sent to pathology (Figure 3B). Frozen sections of marrow contents from proximal and distal margins were negative for tumor.

The contralateral fibula was simultaneously harvested by a microsurgeon for an intercalary vascularized bone graft. The graft was cut to the appropriate size and the proximal and distal ends of the graft were burred down and impacted into the medullary canal on either end of the remaining humeral shaft. Fixation was achieved with quadricortical small fragment screws and a long proximal humerus plate (Figure 3C). Microvascular anastomoses were performed between the peroneal artery and vein and large branches of the brachial artery and vein. Muscle flaps were then reattached to the plate or periosteum and the wound was closed with a drain in place.

Final pathology confirmed Ewing Sarcoma variant characterized by EWSR1-NFATC2 fusion protein with negative margins and 50% tumor necrosis.

Postoperative Course

The patient remained non-weight bearing on the left upper extremity in a shoulder immobilizer for 3 weeks and weight bearing as tolerated on the right lower extremity in a CAM boot. The patient was neurovascularly intact and was discharged home on postoperative day 5. His staples were removed and range of motion was initiated three weeks postoperatively.

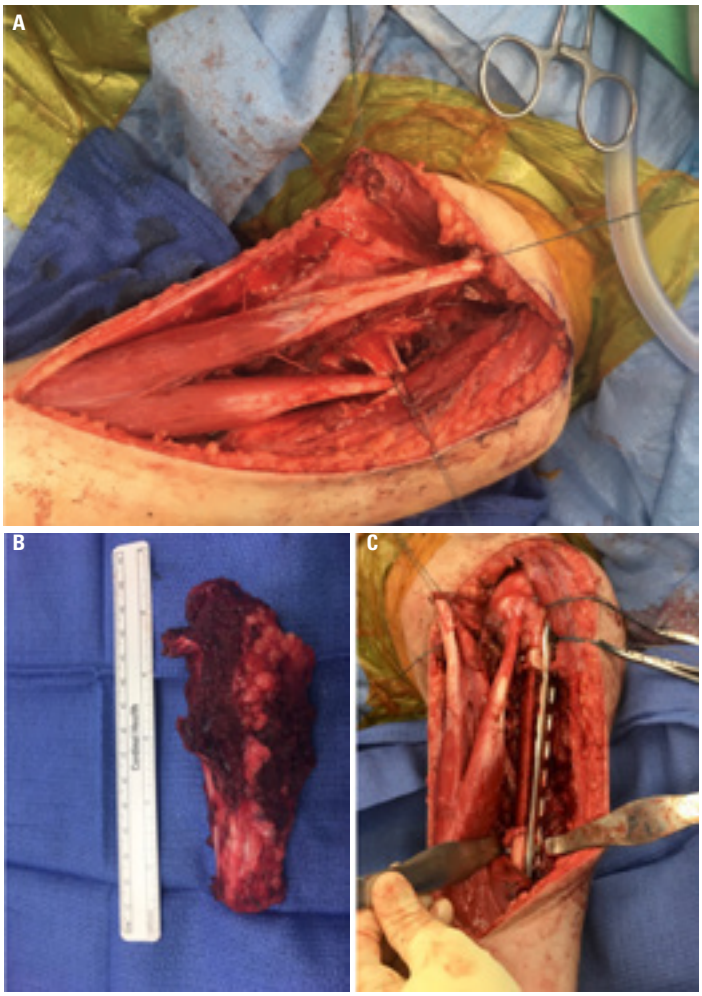

Figure 3. Intraoperative photos depicting **(A)** surgical approach, **(B)** explanted tumor, and **(C)** intercalary fibular graft.

At this time he restarted chemotherapy and completed an additional 7 cycles. The final cycle of ifosfamide and etoposide was deferred due to neutropenia and bacteremia leading to admission for septic shock.

The patient followed up at regular intervals postoperatively without wound complications or evidence of tumor recurrence at one year. Imaging demonstrates complete incorporation of the graft without hardware complications (Figure 3). Exam is notable for full forward flexion, extension, and external rotation of the shoulder and a 20 degree loss of abduction. He has normal sensation in all distributions and appropriate resisted strength. The patient has returned to full activities without pain or functional limitations.

Discussion

Ewing sarcoma is a small round cell sarcoma that is associated with significant morbidity and mortality in the pediatric population. It is most often caused by a translocation of the Ewing sarcoma breakpoint region 1 (EWSR1) gene on chromosome 22 and a member of the E26 transformation-specific (ETS) family of transcription factors on chromosome 11 leading to the formation of a fusion protein, most often EWSR1-FLI1. However, rare histological variants have been

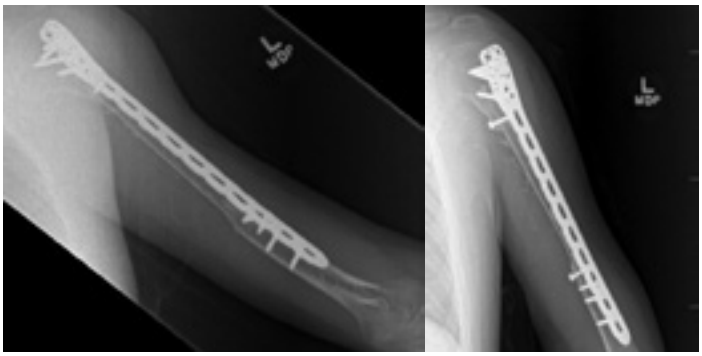

Figure 4. X-rays obtained 10 months after surgery demonstrating graft incorporation.

reported involving fusion to NFATc2 gene, as is seen in this case[2]. These variants exhibit strong cytoplasmic staining with CD99 and dot-like positivity with AE1/AE3. Cells are arranged in nests embedded in myxoid stroma and, unlike classic Ewing sarcoma, the tumor cells are pleomorphic with enlarged nuclei and prominent nucleoli.

The clinical significance of this genetic variant is not well understood. Multimodal treatment approaches with aggressive chemotherapy and radical surgical resection are the cornerstone of treatment. Advances in these techniques have led to limb salvage surgery replacing amputation for the treatment of upper extremity sarcomas without negatively impacting survival. Ultimately, the fundamental goals of limb salvage surgery in the upper extremity are to adequately resect the tumor, preserve hand function, and maintain a survival rate at least equal to that of amputation[3].

There are a variety of reconstructive options available, including prosthetics, allografts, and autografts. While prosthetics permit early use of the extremity, they are at risk of infection or mechanical complications that may require revision surgery, especially in young patients.

Reconstruction with vascularized biological grafts is an attractive alternative given their ability to remodel in response to biomechanical cues and permit longitudinal growth in pediatric patients if the physis is preserved. Free vascularized fibular grafts are the most popular choice for filling segmental defects due to their versatility and low donor site morbidity, however vascularized rib and iliac crest grafts are also reconstructive options[4]. Vascularized autografts are also at lower risk of fracture and infection than allografts and have a higher rate of union[5,6].

The most common complications seen following free vascularized fibula autograft for upper extremity reconstruction are fracture (11.7%), nerve injury/palsy (7.5%), and infection (5.7%)[7]. Although the fibula hypertrophies when used for reconstruction of intercalary defects of the femur and tibia, the rate of fracture is significantly greater than in the upper extremity. Capanna et al. describe the use of an allograft shell with an intramedullary vascularized fibula to create a graft with greater structural integrity and thus mitigate this risk in lower extremity reconstruction[8,9].

Conclusion

Ewing sarcomas are the second most common malignant primary bone sarcomas in the pediatric population. Treatment depends on wide surgical resection (and/or radiation therapy) for local control and chemotherapy for systemic control. Vascularized free fibula grafts are well suited for reconstruction of large segmental defects and offer a limb sparing approach without increasing the risk of tumor recurrence. This case highlights the typical treatment course for a patient who underwent limb salvage with free vascularized fibular autograft. His ability to return to normal activities without significant deformity or functional limitation exemplifies the current shift in focus to a patient centered approach for the management of complex diseases.

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