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Solitary Metastatic Lesion of the Tibia from Clear Cell Renal Carcinoma: A Case Report of Segmental Skeletal Resection, Intercalary Allograft Over Reamed Nailing and Soleus Flap Interposition

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Male, 54
Final Diagnosis: Metastatic lesion of tibia from renal cell carcinoma
Symptoms: Mass in anterior tibia • pain
Medication: —
Clinical Procedure: Resection and allograft interposition
Specialty: Orthopedics and Traumatology

Objective: Unusual clinical course

Background: Renal cell carcinoma (RCC) is the most common malignancy of the kidney, with clear cell (ccRCC) subtype identified in 85% of the cases; one-third of these patients experience synchronous metastatic disease, while 20–30% of the remaining patients develop metachronous metastatic RCC. The axial skeleton (pelvis and sacrum) is the second most common location (following the lungs), with a reported incidence of 35%. Diaphysis of the long bones is rarely involved, with the tibia being an even rarer site of metastasis.

Case Report: We present a rare case of solitary diaphyseal tibial metachronous metastasis from RCC in a 54-year-old male that appeared 8 years after nephrectomy without any previous evidence of disease. He underwent segmental skeletal resection, intercalary allograft over locked reamed intramedullary nailing, and soleus flap coverage. Thirty months later he presented with hardware failure and nonunion at the distal part of the allograft site. He was successfully treated with exchange nailing, fibular osteotomy, and bone grafting, showing excellent clinical and radiological outcome without any evidence of recurrence 5 years after the index operation.

Conclusions: Wide resection and biological reconstruction using intramedullary nailing and incorporated allograft is a good option for metachronous solitary RCC tumors.

MeSH Keywords: Allografts • Bone Nails • Carcinoma, Renal Cell • Neoplasm Metastasis • Tibia

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Background

Renal cell carcinoma (RCC) is the most common malignancy of the kidneys, with clear cell (ccRCC) subtype identified in 85% of these cases; one-third of these patients experience synchronous metastatic disease and 20–30% of the remaining patients have metachronous metastatic RCC [1,2]. Tibia is a very rare site of RCC metastasis: Zekri et al. [3] in a recent study of 103 patients with advanced RCC and metastatic bone disease reported that the pelvis and ribs were involved in 48% of the patients, followed by the spine in 42%, followed by the long bones and skull. Fottner et al. [4] described only 3 cases of tibial metastasis in 101 cases (2.97%) with RCC and found that patients with solitary types, age <65 years old, absence of pathologic fracture, and tumor-free resection margins had a better survival rate compared to patients with multiple metastases. Patients with solitary bone metastasis from RCC have the best prognosis, with a 5-year survival rate between 35% and 60% [5]. Due to the longer survival of these patients, some authors recommend a surgical approach aiming at curative rather than palliative outcome and implant stabilization to prevent local disease progression [6,7]. Here, we present a rare case of solitary tibial metachronous metastasis from RCC in a 54-year-old male that appeared 8 years after nephrectomy without any evidence of disease until then. Segmental skeletal resection, intercalary allograft over locked reamed intramedullary nailing, and soleus flap coverage led to a successful clinical and radiological outcome without any evidence of recurrence for 5 years postoperatively.

Case Report

A 54-year-old man presented in October 2013 to the Department of Orthopedic Oncology with a palpable mass at the middle of his left tibia. He had noticed it a month ago but did not complain of any difficulty weight-bearing or walking, nor was there nocturnal pain or systemic illness. The mass was painful on palpation without any signs of local inflammation. He had undergone a right nephrectomy 8 years ago due to clear cell RCC, but he remained asymptomatic without any evidence of recurrence according to his most recent computed tomography (CT) screening (brain, chest, abdomen) performed 1 year ago. Plain anteroposterior and lateral radiographs of the tibia revealed a small lucent lesion at the midshaft (Figure 1A, 1B). A complete diagnostic imaging workup was done, including computed tomography (CT) of the tibia and staging protocol (brain-chest-abdomen), 3-phase bone scintigraphy, and magnetic resonance imaging (MRI) (Figure 1C–1E). No other possible metastatic lesions were identified. The CT and MRI scans demonstrated a medullary osteolytic lesion of the middle tibia, measuring 1.5×1 cm in size, breaching the nearby anterior tibial cortex and involving the soft tissues of the anterior compartment. There was homogeneous enhancement with the use of paramagnetic material. Moderate recruitment on the tibia lesion was noticed on the bone scan but the rest of the skeleton was normal. Open biopsy of the lesion showed clear cell carcinoma, morphologically compatible with metastasis of the renal carcinoma. After detailed discussion of all available therapeutic options, the patient consented to biological surgical treatment, including wide resection, intercalary allograft over nailing, and soleus flap interposition. The operation took place 3 weeks after the biopsy under general anesthesia (Figures 2, 3). Tibial traction was applied through a Steinmann pin placed at the calcaneus. A longitudinal oval incision incorporating the previous biopsy scar was performed. The tumor was recognized and a 7-cm bone segment was resected with transverse osteotomy using an oscillating saw; the surrounding soft-tissue mass was also excised to obtain healthy margins. With the tibia under traction, a guide wire was inserted through the patellar tendon and its central position was confirmed with C-arm fluoroscopy in both anteroposterior and lateral views. Both the proximal and distal parts of the tibia were reamed to a diameter of 12 mm and a flexible GK nail (Grosse & Kempf® Locking Nail System – Stryker, Kalamazoo, Michigan, USA), 11 mm in diameter and 345 mm in length was inserted. A matched femoral allograft that had been previously thawed in antibiotic solution was incorporated into the tibia. The allograft was trimmed at both edges with a burr to achieve a more cylindrical shape corresponding to the tibial cortex in both sides. Distal interlocking was performed first, and with a backslap stroke the intercalary allograft was further compressed. The nail was finally locked proximally with another 2 screws. The soft-tissue defect was covered with medial soleus flap and skin grafting from the ipsilateral femur. The duration of the operation was 2 hours and there was no significant blood loss or need of transfusion. The histological examination of the entire tibial specimen confirmed the presence of metastatic ccRCC being resected on “clear margins”. After oncological consultation, no adjuvant chemotherapy or radiotherapy was proposed to the patient. Partial weight bearing was initiated on the 2nd postoperative day, with instructions to the patient to increase weight bearing progressively and attain full weight bearing at 6 weeks. The patient was followed up regularly, having no clinical complaints and showed progressive healing of the allograft-host junction, especially in the proximal part; the distal part showed delayed union but the patient had no problems during activities of daily living. Thirty months later (March 2016), he experienced sudden pain at the distal tibia and inability to bear weight; radiological examination revealed hardware failure with breakage of both the nail and distal screws due to nonunion at the distal part of the allograft-host junction (Figure 4A). The patient underwent reamed exchanged nailing using a GK nail (12-mm diameter and 330-mm length) with distal interlocking only, fibular osteotomy, and application of iliac bone cancellous autograft (Figure 4B).

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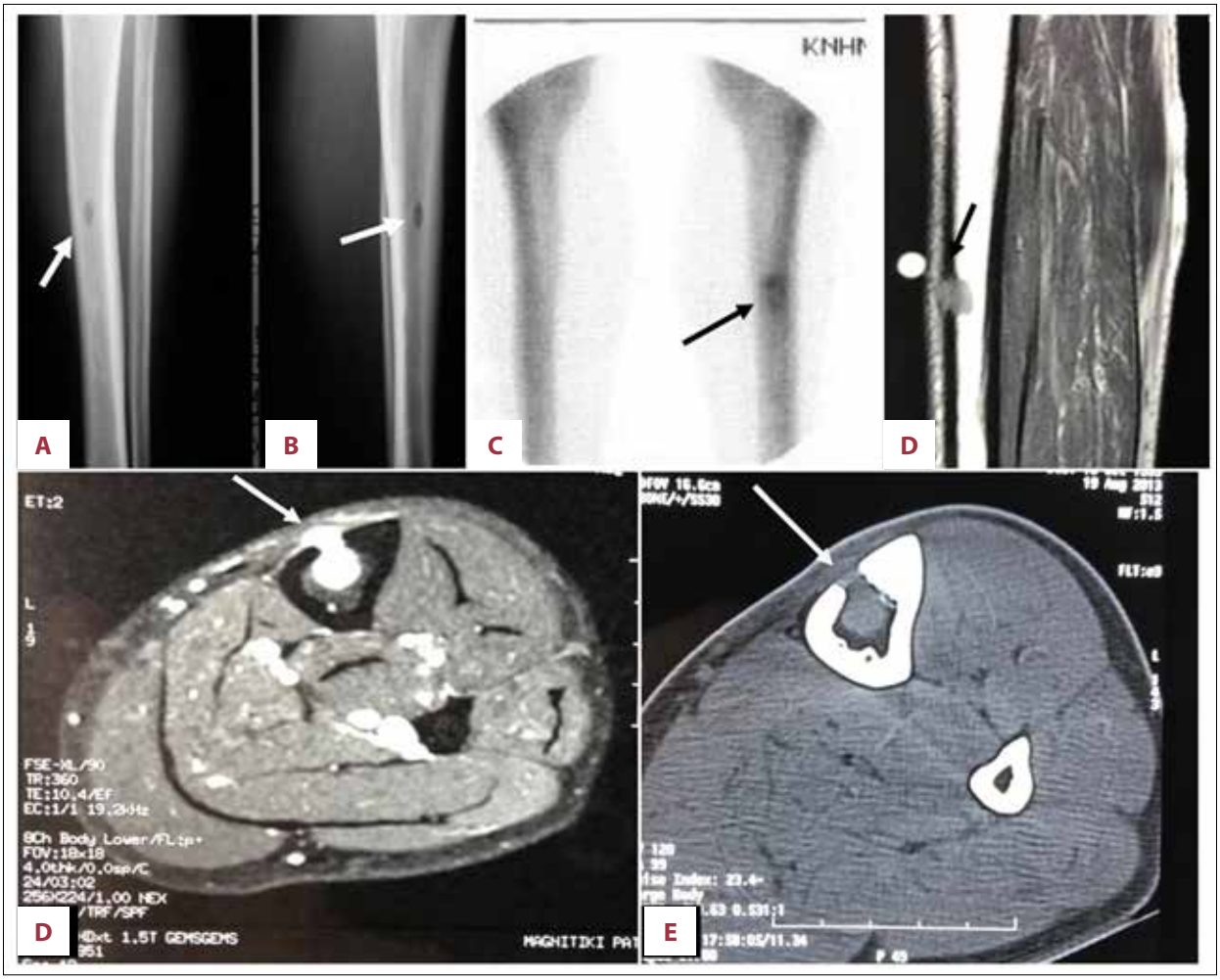

Figure 1. (**A, B**) Anteroposterior and lateral x-rays of the left tibia indicating a small lucent lesion at the midshaft. (**B**) Bone scan of the entire skeleton demonstrating relatively high intake from the lesion in the tibia. (**C, D**) Sagittal and axial T1- and T2-weighted MRI images showing abnormal low and high signal, respectively, with disruption of the anterior cortex. (**E**) Axial CT scan showing a medullary low signal lesion of the middle tibia, measuring 1.5×1 cm in size, breaching the nearby anterior tibial cortex and involving the soft tissues of the anterior compartment.

No major complications where noticed during the postoperative period and he was allowed to do full weight-bearing thereafter. At his last follow up 2 years later and 5 years after the first operation, the patient was free of tumor disease and showed solid union (Figure 4C), unrestricted mobilization, no leg-length discrepancy, and a Revised Musculoskeletal Tumor Society Rating Scale of 27/30. This scale was introduced in 1993 by Enneking et al. [8] (*https://faoj.files.wordpress.com/2009/03/fosstab1.pdf*) and assigns numerical values (0–5) for each of 6 categories: pain, and function and emotional acceptance in upper and lower extremities; supports and walking and gait in the lower extremity; and hand positioning, and dexterity and lifting ability in the upper extremity.

Discussion

Limb-salvage procedures without compromising fundamental oncological principles have become the rule rather than the exception in patients with solitary metastatic bone tumors; early diagnosis, advanced imaging modalities, refined surgical reconstructions, and multidisciplinary approaches have contributed to a significant increase of the long-term survival of these patients, who now demonstrate survival rates up to 80% [9].

Metastasis in RCC occurs most commonly to the lungs, followed by bone involvement in 20–35%, lymph nodes, liver, adrenal glands, and brain. In metastatic disease, the median survival rate of patients is about 8 months, with 50% mortality rate within the first year, while the 5-year survival rate is only 10% [10]. Skeletal involvement is usually an aggressive, lytic

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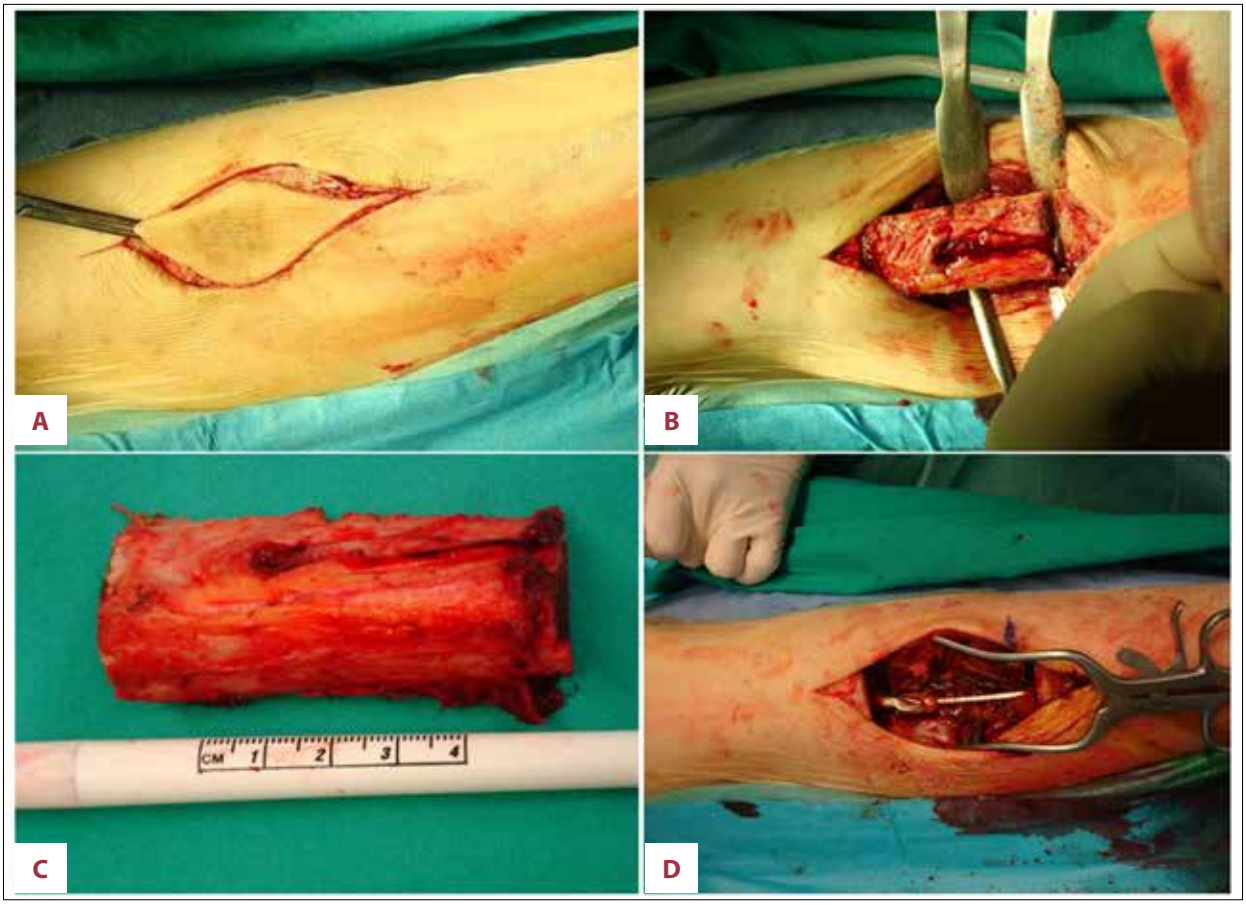

Figure 2. (**A**) Skin incision including the area of previous biopsy. (**B**) Osteotomy of the tibia at both sides with an oscillating saw (7 cm length). (**C**) Resected part of the tibia. (**D**) Reaming at both parts of the tibia over guide wire.

process which causes substantial morbidity through skeletal related events (SREs: pain, impending fracture, spine cord compression, hypercalcemia, and pathological fracture). The tibia and the diaphysis of long bones in general are a very rare site of involvement [3,4]. In a recent case report (2012) of synchronous metastatic tibial diaphysis fracture in the presence of bilateral renal cancer with liver deposits, a 75-year-old male patient was treated with prophylactic intramedullary nailing [11]. In a more recent (2016) case report [12] of concurrent tibial and ankle metastasis in a 67-year-old male who presented 1 year after radical nephrectomy and was treated with above knee amputation, the authors mentioned 23 similar cases in their literature review. Laitinen et al. [13] reported the survival and complication rates of skeletal prosthetic reconstruction in 206/253 patients with metastatic RCC and performed this kind of treatment in only 2 tibial diaphyseal cases (1.3%). Our patient had a small lucent lesion in the tibial diaphysis that presented 8 years after nephrectomy. In general, prognostic factors for a good clinical outcome include young age, solitary metastasis, no pathologic fracture, tumor-free resection margins, and long interval from initial RCC appearance, which were all met in our case [4–6,13].

There are several options to achieve reconstruction and stabilization of segmental intercalary diaphyseal defects: (1) allografts [14], (2) free or pedicled vascularized fibula grafts [15], (3) combined allograft and vascularized fibula [16], (4) extracorporeal devitalized autograft [17], (5) distraction osteogenesis [18], and (6) segmental intercalary endoprosthesis [19,20].

The goal of any type of reconstruction is to achieve local control of the disease while maintaining limb function. Our decision to apply biological reconstruction with intercalary allograft was mainly based on tumor location (tibial diaphysis), size (small, inside the medullary canal with limited soft-tissue compromise) and type (solitary RCC), the young age of the patient, the long interval of metastatic emergence (8 years), and the absence of metastatic disease in other organs. Wide excision (7 cm) was performed in accordance with the study by Fortner et al. [4], which found a better Kaplan-Meier survival curve in patients with a tumor-free resection margin. For the same reason, we did not use preoperative embolization; the latter provides tumor devascularization, controls hemorrhage, reduces intraoperative blood loss, and facilitates curettage, but if wide resection is planned, there is no indication because it would lead

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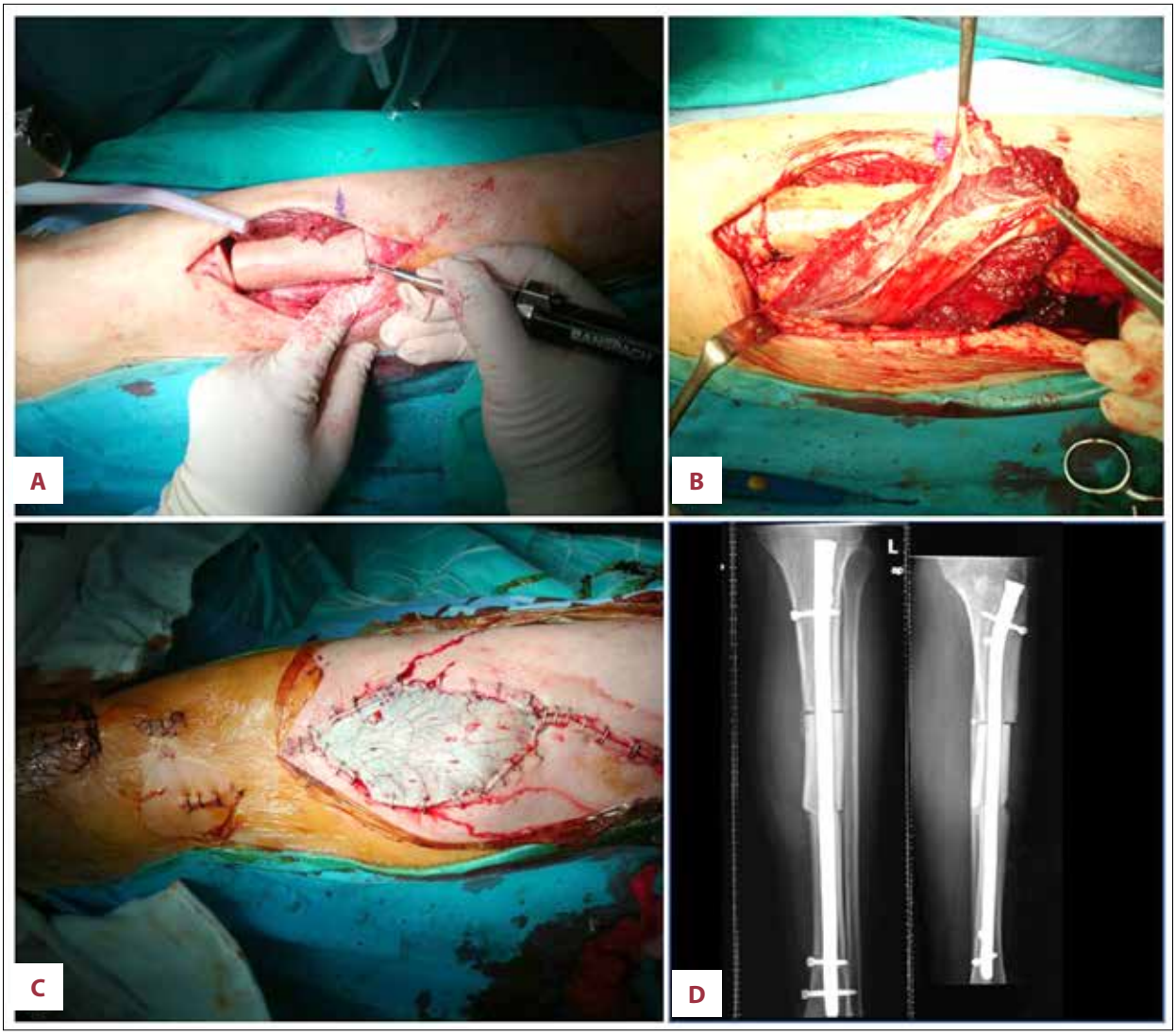

Figure 3. (A) Interposition of the allograft over the nail and trimming of both graft edges for better matching to the host bone. (B) Preparation and placement of the muscle flap, (C) The skin defect was covered with the skin graft. (D) Postoperative anteroposterior and lateral x-ray of the tibia showing good graft incorporation and adequate compression.

to marked hypervascularity in the area surrounding the tumor, which would result in heavy bleeding during surgery [21].

Segmental endoprosthesis is another non-biological alternative for intercalary reconstructions that offers early weight bearing, rapid rehabilitation, and immediate stability. Nevertheless, healing is ignored and a significant risk of infection, periprosthetic fracture, aseptic loosening, and mechanical wear has been reported [13,19,20]. The 10-year survival of segmental endoprostheses ranges from 63% to 80%, with a reported 17–33% rate of implant failure [20,22]; therefore, in our opinion that method should be applied in elderly patients with poor healing capacity, patients with metastatic bone disease, or those with a very short life expectancy, in whom instant weight bearing and full function are more important than construct maintenance.

The use of allograft reconstruction in oncological surgery was first reported 50 years ago and has been popular ever since, especially with the establishment of organized tissue banks and the minimization of justifiable concerns regarding immunogenicity, antigenicity, and potential disease transmission. Their main advantages are preservation of bone stock, biological graft incorporation, adequate attachment of salvaged soft tissues, and initial mechanical strength [23]. Five-year allograft survival rate is around 80% [14,23,24], but up to 70% of patients will require additional surgical procedures due to the common "triad" of complications – infection, fracture, and nonunion – that usually tend to occur within 3 years of the index procedure, as in our case (nonunion), with the construct becoming much more stable if it survives this crucial period of time. Nonunion rate varies from 8% to 44% (higher for diaphyseal junctions);

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Figure 4. (**A**) Radiological examination at 30 months showing nail and screws breakage and hypertrophic nonunion at the distal part of the allograft. (**B**) Postoperative x-ray after exchange nailing and fibula osteotomy. (**C**) Final x-ray at 5 years and 2 years after revision, showing excellent graft incorporation, no signs of recurrence, and good skin condition.

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fractures occur in 15–19%, and infection occurs in 11.5–16%, most commonly within the first year [14,23–25]. Allografts unite with the host bone through external callus formation, which is directed to the surface of the allograft. As the allograft is only partially incorporated to the host, a stable fixation either with compression plating, intramedullary nailing, or both is of fundamental importance. Plate fixation allows for more controlled compression of the host osteotomy site but carries a higher risk for fracture due to screw penetration through the allograft, while intramedullary fixation is less invasive but can induce distraction at the host-allograft junction [26]. In an already compromised healing environment, a residual gap may lead to delayed union or nonunion, as in our case. Allograft fixation with IM nailing has been considered a negative factor for allograft union in comparison to plate fixation [27]. However, other studies [28] found no statistically significant difference between plate and nail fixation for host-allograft union. The use of "compressive nails" that allow internal compression of the junction site seems to promote healing, with a reported union rate of 87% [29]. The use of a larger IM nail with dynamic distal interlocking at the revision operation of our patient attained healing of the distal osteotomy site.

Apart from mechanical stability, biological enhancement of the allograft-host junction is another important factor to promote healing and can be achieved with the addition of cancellous bone autograft, bone morphogenic proteins, autologous bone marrow aspiration, bisphosphonate treatment, and muscular flaps, as in our case. Tumor resection in our case resulted in a soft-tissue deficit; the use of a soleus flap filled up the void and also covered the allograft, thus protecting it from exposure and infection. Muscle has been also found to promote fracture healing, not just because of the increased blood flow [30] but also due to the migration of muscle-derived stroma cells to the osteotomy site and their subsequent differentiation to osteoblastic cells [31].

Conclusions

Our patient was an ideal candidate for biological reconstruction as he presented with all favorable prognostic factors for aggressive surgical treatment. Nonunion or delayed union, which is a common complication of allografting, can be successfully treated with exchange nailing, leading to a good outcome.

Conflict of interest

None.

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