CASE REPORT

Induced-membrane femur reconstruction after resection of bone malignancies: Three cases of massive graft resorption in children

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Accepted: 2 January 2013

KEYWORDS
Osteosarcoma;
Children;
Bone reconstruction;
Induced membrane;
Masquelet;
Complication

Summary Bone reconstruction after surgical resection of bone malignancies in children remains a difficult challenge. Induced-membrane reconstruction as described by Masquelet et al. was originally reported in traumatic or septic bone defects and is now adapted to this field. We report here three cases of massive femoral graft resorption requiring surgical revision in two boys aged 3 and 6 years and a 9-year-old girl. Hypotheses include the long delay between the two stages, nature of the bone graft, high varus loads specific to this location, and lack of stability of the fixation. This technique has recently provided promising preliminary results when applied to the field of bone tumours. However, reconstruction of the femur seems to be specifically associated with a risk of graft resorption. Identification of the origin of this major complication is needed to amend the technique or its indications.

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Introduction

Advances in chemotherapy and medical imaging, together with recommendations to perform extensive resection surgery in children with bone malignancies, now produce 10-year survival rates of 60 to 92% and ensure limb salvage in 85% of cases [1,2]. Once the tumour is removed, the bone must be reconstructed [3,4]. Reconstruction can be
achieved using a vascularised fibular graft and/or a segmental allograft, an extracorporeally irradiated autograft, bone transport, chondrodiastasis, or a reconstruction prosthesis [4,5]. All these techniques are associated with complications [4,5]. The induced-membrane technique developed by Masquelet and Begue allows two-stage reconstruction of long bones and has produced good outcomes in patients with defects due to trauma or infection [6]. In recent years, this technique has been used after bone malignancy resection in children. Advantages include relative simplicity, a short reconstruction time (independently from the resection time), and early weight bearing after the first stage. However, the second stage, i.e., the implantation of a bone graft, is best delayed until adjuvant chemotherapy is completed, as chemotherapy agents have adverse effects on osteoblasts and induce neutropenia, which increases the risk of infection. Promising preliminary results have been reported, although the limitations of the induced-membrane technique remain unclear [7–9].

Here, we report three cases of massive bone graft resorption in children treated for femoral bone tumours.

Case no. 1

This 3-year-old boy had an Ewing’s sarcoma of the right femur (Fig. 1A). Resection of a 15-cm segment of the femoral diaphysis (70% of the total femoral length) with confirmed R0 margins was performed. A cement spacer was implanted and elastic stable intramedullary nail fixation was performed (Fig. 1B). Weight bearing was not allowed before the second stage, which took place 6 months later, after adjuvant chemotherapy completion. An autologous cancellous iliac-crest bone graft buttressed with a medial tibial strut was used (Fig. 1C). Rapid resorption of half the bone graft occurred, with failure of the construct and telescoping 6 months after the second stage, before the resumption of weight bearing. Surgical revision for repeat bone grafting was performed (Fig. 1D). The patient was able to resume weight bearing 6 months later. Two further surgical procedures were required, for wire shortening then replacement of a broken wire after 20 months. After 3 years, the patient was able to walk with full weight bearing; the limb length discrepancy was 6 cm and bone healing was considered incomplete.

Case no. 2

In this 6-year-old boy, an osteosarcoma of the left femur required distal transepiphysial resection with removal of a 20-cm segment (50% of the total femoral length) (Fig. 2A). Histology showed R0 margins. The first stage of the reconstruction procedure consisted in implanting a cement spacer and intramedullary wires (Fig. 2B). Partial weight bearing was resumed after 1 month. The second stage was performed 6 months later, after the completion of adjuvant chemotherapy. An autologous iliac-crest cancellous bone graft augmented with femoral-head cancellous bone allograft was implanted. Fixation was with an intramedullary femorotibial nail for knee arthrodesis (Fig. 2C). After 1 month, partial weight bearing was resumed. The graft underwent gradual resorption, starting at its proximal end after 3 months and involving the proximal two-thirds after 6 months (Fig. 2D). Revision surgery was performed for repeat bone grafting consisting in implantation of a contralateral tibial strut, femoral-head cancellous bone allograft, and tricalcium phosphate granules. Full weight bearing was resumed 3 months after the revision procedure and bone union was considered complete after 18 months. A fracture of the middle third of the femoral shaft and intramedullary nail occurred:

Figure 1 Case no. 1. Ewing’s sarcoma of the right femur in a 3-year-old boy. Lateral radiographs. A. Before tumour resection. B. After the first stage of the reconstruction procedure. C. After the second stage of the reconstruction procedure, performed 6 months later. D. Proximal bone graft resorption and telescoping 6 months after bone grafting.
Induced-membrane femur reconstruction after resection of bone malignancies

Figure 2  Case no. 2. Osteosarcoma of the left femur in a 6-year-old boy. A. Radiograph before tumour resection. B. Radiograph after the first stage of the reconstruction procedure. C. Radiograph after the second stage of the reconstruction procedure, performed 6 months later. D. Proximal bone graft resorption 6 months after bone grafting.

despite continuity of the femur, a lateral defect resulted in fatigue failure of the nail. Revision surgery was performed for reaming of the femur followed by fixation with a locking intramedullary nail and implantation of a femoral-head cancellous bone allograft graft into the fracture site. Healing was still on-going 2 years after the initial procedure.

Case no. 3

A 9-year-old girl sustained a fracture of the left femur due to an osteosarcoma. Because of initial external fixation, treatment required extensive resection resulting in removal of a 22-cm segment (60% of the total femoral length), with confirmed R0 margins (Fig. 3A). A cement spacer and a locked intramedullary nail were used for the first reconstruction stage (Fig. 3B). Partial weight bearing was resumed after 1 month. The second stage performed 7 months later, after adjuvant chemotherapy completion, involved the implantation of an autologous cancellous iliac-crest bone graft augmented with femoral-head cancellous bone allograft. The internal fixation was left unchanged (Fig. 3C). Only partial weight bearing was possible after 6 months. Gradual graft resorption was first noted 3 months after the second stage. After 11 months, complete graft resorption and mechanical failure of the construct required revision surgery (Fig. 3D).
The nail was removed and a locking plate was used to achieve fixation. Another cement spacer was implanted. Full weight bearing was possible after 2 months. After 14 months, the spacer was removed and an autologous vascularised fibular graft fitted into an allograft was implanted. In the immediate postoperative period, necrotising myositis of the donor site on the ipsilateral leg required vacuum dressings and repeated debridement under general anaesthesia. At last follow-up 2 years and 8 months after tumour resection, healing was complete and full weight bearing was possible with predominant contact on the lateral edge of the foot due to residual partial necrosis of the anterolateral leg compartment.

**Discussion**

Massive graft resorption is a serious complication of induced-membrane reconstruction. To our knowledge, our three cases are the first reported to date. Several hypotheses can be put forward to explain this complication.

First, some of the recommendations made by the developers of the induced-membrane technique [10] were not followed. The interval between the two stages should ideally be six to eight weeks. We chose to wait until the end of the adjuvant chemotherapy, as antimitotic agents adversely affect bone grafts [11,12]. The histological and immunohistological characteristics of the membrane after 6 months

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**Figure 3** Case no. 3. Osteosarcoma of the left femur in a 9-year-old girl. A. Radiographs before tumour resection: pathological fracture managed by external fixation. B. Radiograph after the first stage of the reconstruction procedure. C. Radiograph after the second stage of the reconstruction procedure, performed 7 months later. D. Gradual complete resorption of the bone graft 9 months (left) and 11 months (right) after the second stage of the reconstruction procedure.
have not been studied and may be altered. Masquelet and Begue specified that very small fragments of autologous cancellous bone should account for at least two-thirds of the total bone graft volume, and they did not advocate adding a cortical bone graft [10]. In our patients, the large size of the defect required the addition of cancellous bone allograft amounting to half the total graft volume in 1 case and of a tibial strut graft in another case.

Second, experimental studies have established that insufficient stability is the leading risk factor for bone graft non-union [13]. Although an intramedullary nailing was used in two of our three patients, the short length of the proximal segment may have limited the stability of the construct. At the femur, the divergence between mechanical and anatomical axis results in high varus loads. The high rate of mechanical complications at the femur has been underlined previously [7].

Third, in all three patients a large proportion of the femur (50 to 70%) was removed. Both mechanical and vascular considerations suggest that this fact may have precluded bone graft integration. Thus, the defects in our patients may have exceeded the reconstruction capabilities of the induced-membrane technique.

Finally, bone graft resorption might have been related to a local tumour recurrence or infection. This hypothesis is highly unlikely, as results were negative from the biopsies and microbiological specimens obtained during revision surgery in all three patients. Massive bone graft resorption may be specific of femoral lesions, although good results have been reported with this technique applied at the femur [7,9].

The induced-membrane technique has several advantages for bone reconstruction after the resection of limb bone malignancies in children but is also associated with major complications. Studies of larger case-series will help to define the limitations of this technique.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.