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Original Article

Complications of massive allograft reconstruction for bone tumors

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Abstract

BACKGROUND: Since the evolution of multi-drug chemotherapy and radiotherapy and new sophisticated surgical techniques, limb salvage and reconstruction, rather than amputation, has become the preferred treatment for patients with bone tumors. One option is allograft replacement. Although allograft has several advantages, it is not without complications. This study was performed to observe these complications in a group of patients treated with allograft replacement for bone tumor resection. The purpose was to gain an overview of the factors predisposing to these complications to minimize their occurrence.

METHODS: This retrospective study was performed on patients with benign aggressive and malignant bone tumors undergoing limb reconstruction with allograft between 1997 and 2005 in Al-Zahra and Kashani Hospitals in Isfahan, Iran. Data was collected from patient files, clinical notes, radiographs and a recent physical examination. Complications including local recurrence, fracture of allograft, fixation failure, nonunion, infection, skin necrosis and neurological damage were recorded.

RESULTS: Sixty patients including 39 males and 21 females were studied. The mean age of patients was 23 ± 11.7 years. The mean follow-up interval was 28.1 ± 12.4 months (mean ± SD). Complications were allograft fracture in 20%, local recurrence in 16%, fixation failure in 11%, nonunion in 6%, infection in 6%, skin necrosis in 6%, and peroneal nerve palsy in 1% of cases. Most local recurrences (60%) were those with a mal-performed biopsy. Most allograft fractures occurred when a short plate was used.

CONCLUSIONS: Allograft replacement for bone tumors remains a valid option. To avoid complications, biopsy should be done by a trained surgeon in bone oncology. A long plate is recommended for fixation. Sterility and graft processing must be optimal. Autogenous bone graft must be added at host-allograft junction.

KEY WORDS: Bone tumors, bone allograft, limb reconstruction.

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Macewen (1881) and Lexer (1908) were the first to use osteoarticular allograft [1-3]. In the following 50 years, this type of operation was rarely performed until 1954 when Herndon and Chase reported the use of fresh and frozen allograft in dogs [4]. Allograft replacement for bone tumors has developed as an option for limb reconstruction in tumor surgery.

Since the evolution of multi-drug chemotherapy and radiotherapy and the new sophisticated surgical techniques, limb saving and reconstruction, rather than amputation, has become the preferred treatment for a large population of patients with bone tumors [5,6]. Choosing between amputation and limb salvage depends on several factors, including functional outcome, survival, morbidity and

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psychological issues [5]. The advantages of allograft over prosthetic replacement are as follows [5,7-9]:

1- More anatomic and natural fitness of allograft

2- Preservation of ligaments and muscles and reconnection of these structures provide greater stability and function.

3- Preservation of one growth plate, especially around the knee, where the growth rate is maximal, by replacing distal femur only, or proximal tibia only. This is critical in young patients where prosthetic replacement of both sides would lead to significant limb shortening. By preparing a long graft, adjustment can be made through the operation with respect to the length needed for graft replacement.

4- Progressive incorporation of allograft by the host.

Besides other challenges of limb salvage procedures in tumor surgery, allograft has its own drawbacks. Complications arising from such procedures are the major determinants limiting their success. Possible disease transmission and a high risk of infection, fracture, resorption and nonunion are examples [5, 7, 10, 11]. An overview of these complications is essential to efforts towards minimizing them. Thus, we collected our data and prepared a preliminary article on complications of limb reconstruction for bone tumors, using allograft.

Methods

This retrospective study was performed on 60 patients with benign aggressive and malignant bone tumors who underwent allograft replacement surgery, conducted by the senior author, at Al-Zahra and Kashani hospitals, Isfahan, Iran, between March 1997 and September 2005.

The patients were diagnosed as having a bone tumor by history of pain or mass, physical examination, radiography, CT scan and MRI.

Tc-99 bone scan, chest X-ray and CT scan were performed to detect skeletal and lung metastasis. Then a biopsy was performed to establish the definite pathological diagnosis. A group of 23 patients were referred from other centers after biopsy to undergo the definite procedure. Surgery was then carried out to resect the tumor and replace it with an allograft. Allografts were prepared in the bone bank of Imam-Khomeini Hospital, Tehran, and sterilized using one of the three methods: fresh frozen, gamma irradiation and ethylene oxide. The grafts were complete joints, osteoarticular or intercalary grafts, or were used as a composite with total hip arthroplasty. A tourniquet was used where possible. After wide resection of the tumors, allografts were fixed to the host bone by means of plates and screws or intramedullary nailing. Postoperatively, a splint was used and the patients were given prophylactic antibiotics and discharged from hospital when edema and pain had ceased and wound inflammation subsided. The splint or brace was discontinued when radiological signs of union were seen on serial radiographic examinations. Depending on the type and grade of the tumor, radiotherapy or chemotherapy or both were added to the treatment protocol. Patients were followed weekly for the first few weeks, every month until 3 months, every 3 months during the first 2 years and annually thereafter.

Data, including age, gender, type of tumor and its location, the type of allograft used, and local complications because of surgery (infection, local recurrence, allograft fracture, fixation failure, nonunion, skin necrosis and neurological damage) were collected from patient files, clinical notes, radiographs and a recent examination of the patients. The follow-up intervals were also recorded. For patients who died (usually because of lung metastasis), the follow-up interval was considered until death.

Results

Sixty patients including 39 men and 21 women were operated on and followed. The patients were aged between 13 and 71 years with a mean age of 23 ± 11.7 years (mean ± SD). The follow-up interval was from 6 months to 8 years with a mean of 28.1 ± 12.4 months.

The tumors were 42 osteosarcomas, 5 malignant fibrous histiocytomas, 4 chondrosarcomas, 4 aggressive giant cell tumors, 3 Ewing sarcomas, one adamantinoma and one metastatic carcinoma.

Total joint allograft was used in 4 patients with total involvement of the knee joint (figure 1). Forty-two patients underwent one-sided allograft replacement of the knee joint, including 26 distal femurs (figure 2) and 16 proximal tibias (figure 3). Six Patients underwent an allograft replacement of proximal humerus (figure 4). Five patients had composite allograft-total hip arthroplasty for tumors of proximal femur (figure 5). The distal graft-host junction was fixed by means of the long stem of femoral components. The remaining 3 patients were those with diaphyseal tumors and thus an intercalary graft replacement (figure 6).

Allograft fracture was the most common complication and was seen in 12 patients (20%). Ten patients (16%) suffered from local recurrence. Fixation failure occurred in 7 (11%), and nonunion in 4 (6%) patients. Other complications were infection in 4 (6%) patients, skin necrosis in 4 (6%) patients, and nerve injury (peroneal nerve) in one (1%) patient. Infection was severe (pseudomonas) in 2 patients, hence requiring removal of allograft, implantation of a cement spacer and long-term antibiotics. After eradication of infection, re-operation with allograft replacement was performed. Nonunion was treated with autogenous bone graft with or without revision of fixation. Skin sloughs required debridement and skin grafting of the wound. Fixation failure was managed by replating of the allograft.

Of 10 patients with local recurrence, 6 (60%) were those referred from other centers after biopsy. Of these 10 patients, 7 were managed by repeated wide resection and allograft replacement and the remaining 3 underwent amputation. Patients with allograft fracture underwent repeated allograft replacement.

Figure 1. Osteosarcoma of distal femur involving knee joint treated by a total joint allograft.

Figure 2. Osteosarcoma of distal femur treated by a distal femoral allograft.

Figure 3. Osteosarcoma of proximal tibia treated by a proximal tibial allograft.

Figure 4. Chondrosarcoma of proximal humerus treated by a proximal humeral allograft.

Figure 5. Osteosarcoma of proximal femur treated by a composite allograft-total hip arthroplasty.

Figure 6. Ewing sarcoma of diaphysis of femur treated by an intercalary allograft.

Discussion

Allograft reconstruction for bone tumors remains a valid option. Numerous researches have shown its efficacy in terms of function and survival [6-9,12,13]. However, complications of such an operation are also numerous and cause allograft failure [7,10,11]. Three factors which apparently affect the results most significantly are recurrence, infection, and fracture, together accounting for >85% of failures [6].

In this study, fracture of allograft was the most common complication (20%). The reported prevalence of such fractures ranges from 9% to 19% in the literature, but has even reached 30.2% (Muscolo) [11-13]. A higher incidence of allograft fracture was also reported in relation to screw holes, suggesting that allografts are very sensitive to stress-concentrating defects [13]. It is obvious that non-viable bone becomes sclerotic and prone to repeated stress fractures that propagate and eventually develop into a complete fracture. We, as well as others [11,13] have observed that fracture is more likely with the use of a short plate covering only a portion of the graft, compared to when a long plate or intramedullary nail covering the entire length of the allograft is used. Thus, allograft fracture was more frequent in early operations, but much less in recent ones using a modified technique to span the entire length.

Local recurrence occurred in 10 patients (16%); although somewhat similar to other studies [6,7], this is unacceptable for it is considered as true failure of an operation aimed at eliminating the tumor. However, it must be mentioned that most cases of recurrence (60%) were those that had undergone a badly-performed and non-classical biopsy, usually in another center, prior to the definite procedure. For example, a lateral approach was used to take a sample from a medially placed tumor. The result was the dissemination of tumoral cells that precluded a wide resection at the

time of surgery, thus predisposing to recurrence. Unusual biopsy tracts also led to skin slough and necrosis due to forced unusual flaps created in the definite procedure (6% of patients).

The importance of infection as a devastating complication cannot be overemphasized, for it can lead to repeated operations and probably amputation if the patient survived at all [5,6]. In a recent study performed on 945 patients with allograft reconstruction, infection developed in 12.8% [10]. The frequency of infection in the overall series of massive allografts reported in the literature ranged from 6% to 30% [13].

In the current study, the infection rate was 6% with only 2 cases (3%) of deep infection requiring re-operation. The immunological response evoked by the body is presumably the major cause of infection [6,10].

Allograft is a nonviable, foreign material and given its large size (massive allografts), infection is a probability. An association between infection and chemotherapy or radiotherapy has been controversial [6,10,14]. In addition to adherence to sterility and routine use of prophylactic antibiotics and proper allograft processing, the low infection rate in our series may have been due to the incomplete effect of chemotherapy protocols used in our centers. Immunogenicity and chemotherapy are considered by some to affect the nonunion rate [6,7,13,15]. Reunion is problematic even in fresh fractures where the two ends are alive and rich with blood, much less when one side of the union site is a dead bone. The type of fixation has been considered as a determinant of nonunion by some authors, with plate fixation being the preferred method [13,16]. Nonunion was seen only in 4 patients (6%) in the current study, which we think is acceptable given the overall nonunion frequency and the rates reported by previous studies (17-63%) [6,13]. The cause is probably rigid internal fixation, frequent use of autogenous graft in the host-graft junction, and again, less effective chemotherapy.

Failure of fixation was another problem that occurred in 11% of our patients. In similar studies, the frequency was 10-18% [7,8]. We must note that the same factures that predispose to fixation failure in non-tumor patients work here to promote the fracture of the plate or dislodgment of the screws. The use of meticulous techniques and good quality metals, as well as greater attention to patient rehabilitation will likely help reduce this complication.

Prosthetic reconstruction has advantages such as the maintenance of motion and immediate functional restoration [17-20]. However, although high prosthetic survival rates have recently been reported [17, 18, 21], complications and failure rates have also been high [19,20,22]. Increased emphasis has been placed on biologic reconstruction alternatives because of concerns about the durability of prosthetic materials and because of the increasing survival of patients with sarcoma [7]. It remains for long-term comparative studies to observe the results of allograft versus prosthetic replacement in bone tumor surgery.

Meanwhile, we make the following recommendations to surgeons who decide to use allograft in bone tumor surgery:

1- Perform the biopsy in light of the definite procedure and adhere to the principles of biopsy presented in detail in textbooks [5]. It has been advised that only the surgeon performing the definite procedure should do the biopsy.

2- Protect the full length of allograft, preferably by a long plate with screws along the entire length of the graft.

3- Match the size of the graft to that of the host bone and use rigid internal fixation. Use autogenous bone graft at the junction of host-allograft bone to accelerate union.

4- Pay strict attention to sterility of the graft and the whole procedure. Use prophylactic antibiotics in all cases. We put the graft in a gentamycin or vancomycin solution prior to use in the body.

Finally, these operations should only be performed by surgeons trained in tumor surgery and with a thorough knowledge of local anatomy, techniques, rehabilitation and complications.

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