Clinical Results of Bone Grafting

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Introduction

The clinical usefulness of bone grafting was established before the grafting of other organs and tissues, and it is a therapeutic modality that is being widely used throughout the world. The types of graft bone are classified: autogeneic bone, allogeneic bone, and xenogenic bone, but autogeneic bone, which has no antigenicitiy at all, is far superior in terms of quality as graft tissue. Nevertheless, because of the limited amount of bone that can be collected, it is sometimes insufficient to fill large bone defects, and at such times allogeneic bone grafts or artificial bone is indicated. Xenogenic bone, which is highly antigenic, is hardly ever used anymore.

Pathological conditions considered to require bone grafts include filling bone defects after excision of bone tumors and injuries and filling areas of bone loss when fixation procedures are necessary to restore stability in spinal operations and when revising artificial joints that have become loose.

Bone grafts are established through the following 3 steps. (1) Bone morphogenetic protein (BMP) contained in the extracellular matrix of the grafted bone induces mesenchymal cells in the graft bed to differentiate into cells that have bone-forming ability (osteinduction). (2) Cells derived from the graft bed that were induced to differentiate invade the graft bone and form new bone by using the frame of the graft bone as a scaffold (osteocoinduction). (3) The graft bone is replaced by newly formed bone, and it forms bone having identical morphology.

Autografts

Despite being autogeneic bone, except for some on the cells in the surface layer, almost all of the cells in the bone of the unvascularized free bone grafts that are usually used die. The cells derived from the graft bed, however, invade the graft bone, and osteogenesis occurs with the graft bone serving as the scaffold, and bone grafting is achieved. After being reported to be useful in fixation of the spine about 90 years ago, autografting of bone was widely adopted around the world, and it has become an indispensable operation in orthopedic surgery.

Moreover, as a result of the increasingly widespread use of microsurgery, vascularized bone autograft operations are now being widely performed. Because blood flow has been preserved...
and the cells in the grafted bone are alive, bone formation and bone fusion are very vigorous and there has been a remarkable improvement in therapeutic success in intractable diseases, including congenital pseudarthrosis, in which bone fusion could not be achieved with conventional free autografts. Achievement of bone fusion in the early stage has been demonstrated even when used for reconstruction after wide excision of malignant bone tumors, and its application is becoming increasingly widespread. The most common site used to collect autogeneic bone for free autogeneic bone grafts has been the ilium, and the most common site for vascularized autografts has been the fibula, with the fresh autogeneic bone collected being grafted into the bone defect area immediately.

Allografts

The antigenicity of bone allografts lies in their cellular components, chiefly bone marrow cells and vascular endothelial cells, and the bone matrix has little antigenicity. Even when the cells in the grafted bone are not alive, cells in the graft bed that possess bone-forming ability are induced by BMP. For these reasons, in contrast to autogeneic bone grafts, grafts of stored allogeneic bone in which the cell component has been killed by frozen storage or by freeze drying yields better clinical results than grafting of fresh allogeneic bone. Immunosuppressive drugs are not needed when stored allogeneic bone grafts are used.

Systems and facilities that store allogeneic bone are called “bone banks”. The point of processing and storing allogeneic bone is to maximize preservation of the BMP in the graft bone while attenuating its antigenicity as much as possible. With the frozen preservation method, storing at the lowest temperature possible is advantageous in terms of BMP preservation, but since storing large amounts of graft bone in liquid nitrogen (−196°C) is difficult from the standpoint of both cost and space, deep freezers (−80°C) are usually used. This frozen preservation method preserves bone collected bacteria-free, and is a simple method in that the bone can be taken out and used whenever necessary. It was first adopted in Japan in 1953 in the Department of Orthopedic Surgery of Kyushu University, and since then it has come to be widely used.

Another allograft preservation method, the freeze-drying method, is highly useful because of enabling preservation at room temperature and being convenient for transportation. In Japan, where there are almost always institutional bone banks that collect extra bone during surgery for artificial hip replacement, etc., at own institution and graft it to other patients as needed, because the freeze-drying process is complicated, it has not become as widespread as the frozen preservation method, whereas in the United States, where regional bone banks that supply allogeneic bone to many institutions have developed, the use of freeze-dried bone has become routine because of the need to preserve and transport large amounts of bone.

More time is required before bone grafting to be completed than with autogeneic bone, but there is no doubt about the usefulness of allogeneic bone for large bone defects that cannot be dealt with by means of autogeneic bone. Although for a long time the national health insurance system in Japan did not cover allografting, last year the charge for allogeneic bone graft procedures was finally included in the national health insurance reimbursement list. It is hoped that the charge for the material will also be listed in the national health insurance reimbursement list, the same as the charge for artificial materials.

Current Status of Bone Grafting in Japan

A nation-wide survey on bone grafts performed in Japan from 1985 to 1989 and from 1990 to 1994 was conducted at all training institutions approved by the Japanese Orthopaedic Association. In the latter half of the survey
replies were received from 883 (42%) of the 2,123 institutions surveyed. Large numbers of bone grafts, totaling 87,720, had been performed during 5 years at these institutions, and the number had increased every year (5-year rate of increase: 37.8%). Autografts had been most common, accounting for 81.2% of the total. The target diseases of the bone grafts had been spinal diseases (37%), trauma (26.2%), joint diseases (26.4%), bone tumors (7.9%), congenital diseases (0.9%), and others (1.3%). The most marked increase in the 5-year period was in spinal diseases, and marked increases were also seen in artificial joint surgery and trauma. There were 125 institutions that had bone banks and performed allografting, and while most of them were institutional banks, regional bone banks have shown a tendency to expand in recent years, with the Aichi bone bank being the first.

Prospects for the Future

As is clear from the results of the nationwide survey as well, it seems that the need for bone grafts is going to continue to increase in the future. The inadequate supply of allografts due to the lack of regional bone banks is a problem peculiar to Japan, and it is hoped that regional tissue banks capable of supplying allogeneic tissues, such as heart valves, skin, etc., not just allogeneic bone, to extensive regions will be established. Based on the prospects for BMP research, innovations to artificially accelerate the completion of bone grafting will be necessary. Moreover, allogeneic grafting of life-supporting organs, including liver transplantation, has become widespread in recent years, and the realization of allografting of complex tissues, in which the entire extremities including blood vessels and nerves will be grafted, not just bone, is expected in the future.

REFERENCES