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Abstract

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KEYWORDS: xenogeneic bone, bone grafting, bone neoplasms

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Radiological Long-Term Follow-up of Grafted Xenogeneic Bone in Patients with Bone Tumors

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Radiological findings on the fate of grafted Kiel bone implants for the treatment of bone tumors were evaluated in 25 lesions. The mean follow-up period was 14.8 years, ranging from 5 to 21.8 years. We classified the radiological findings into 4 grades; Excellent (4 lesions), Good (14 lesions), Fair (2 lesions), and Poor (5 lesions). All cases of the Poor grade were polyostotic fibrous dysplasia. The younger the patient at the time of the operation, the more rapidly Kiel bone grafts tended to be incorporated. The grafted bone can become enmeshed in the structure of the recipient bed (Good or Excellent grades) within 10 years in most cases, except in polyostotic fibrous dysplasia.

Key words : **xenogeneic bone, bone grafting, bone neoplasms**

A number of reports concerning bone allografts have been reported outside our country, but xenogeneic bone or biomaterials have been preferred in Japan due to legal or religious problems. The most widely known xenogeneic bone material is Kiel bone, developed by Maatz and Bauermeister at the University Clinic of Kiel in 1950's (1,2). They noted little residual protein in bone taken from a bovine calf following oxidative deproteined by 20 % hydrogen peroxide solution (1,2). Following extensive animal experiments, this was used in a wide variety of sites with varying success rates, and there were high expectations of its use as an excellent bone implant material (3-5). Reports of successful use in cervical anterior interbody fusion have been published (6,7).

However, problems with the xenogeneic implant materials included a lack of osteoinductive activity (8), which interfered with incorporation in the recipient bed. Moreover, immunological problems could not be completely excluded (9). As a result, the use of Kiel bone has recently been reduced as an orthopedic implant. However, some reports indicated that Kiel bone is effective as banked bone when grafted with autogenous bone marrow, or in a hemorrhagic bed (9,10).

Radiological studies on long-term follow-up of the grafted Kiel bone have been limited to a few cases of benign bone tumors (10,11). In this long-term follow-up study, we analyzed the radiological findings following Kiel bone grafting for approximately 10 years. For comparison, grafted bone was examined histologically 6.6 years after the implantation in a case with chondrosarcoma.

Materials and Methods

Twenty-five lesions in 22 patients were followed for 5 to 21.8 years (Table 1). Ten solitary bone cysts (10

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lesions), 8 fibrous dysplasias (2 monostotic types and 6 polyostotic types, 10 lesions), 2 chondroblastomas, 1 non-ossifying fibroma, and 1 chondrosarcoma. Autogenous bone and Kiel bone were grafted together in 1 lesion (case 10), but in all other 24 lesions Kiel bone alone was grafted after curettage. Cancellous Kiel bone was used as a rule. Mean age at the time of the operation was 15.9 years old (ranging 3 to 56 years old), and the mean follow-up period was 14.8 years (ranging from 5 to 21.8 years). Implant volume ranged from 0.6 to 64.4 cm^3 (mean volume 12.8 cm^3). Referring to Terakado's 5 grades classification for radiological patterns of the grafted Kiel bone implants and recipient bed (11), we made a new radiological classification of 4 grades as shown in

Table 1 Patient characteristics of Kiel bone grafted cases

Cases	Diagnosis	Age	Sex	Site	Length of follow-up	Evaluation (Months after operation) 0 1 3 5 10 15 20
1	Solitary bone cyst	3	F	Femur	20 y[a] 1 m[b]	P → G → E
2	Solitary bone cyst	7	M	Humerus	21 y 10 m	P → F → G → E
3	Solitary bone cyst	7	M	Humerus	20 y	P → F → G → E
4	Solitary bone cyst	7	M	Humerus	12 y 7 m	P → F → G
5	Solitary bone cyst	13	M	Femur	5 y	P → F
6	Solitary bone cyst	15	F	Pelvis	15 y 5 m	P → F → G
7	Solitary bone cyst	15	M	Calcaneus	15 y	P → F → G
8	Solitary bone cyst	20	F	Tibia	5 y 2 m	P → F
9	Solitary bone cyst	33	F	Toe	15 y 2 m	P → F → G
10	Solitary bone cyst[c]	56	F	Femur	8 y	P → F → G
11	Chondroblastoma	13	F	Femur	18 y 8 m	P → F → G
12	Chondroblastoma	25	M	Calcaneus	16 y	P → F → G
13	Non-ossifying fibroma	13	M	Tibia	20 y 5 m	P → F → G
				Calcaneus	20 y 5 m	P → F → G
14	Fibrous dysplasia (m)[d]	4	M	Radius	20 y 7 m	P → G → E
15	Fibrous dysplasia (m)	9	F	Tibia	15 y	P → F → G
16	Fibrous dysplasia (p)[e]	1	F	Femur	14 y	P → F → G
17	Fibrous dysplasia (p)	2	M	Tibia	20 y 3 m	P → F → G
			M	Fibula	20 y 3 m	P → F → G
18	Fibrous dysplasia (p)	4	F	Femur	12 y 1 m	P
19	Fibrous dysplasia (p)	7	M	Femur	10 y	P
20	Fibrous dysplasia (p)	19	F	r-Femur	13 y	P
				l-Femur	12 y 2 m	P
21	Fibrous dysplasia (p)	30	F	Tibia	12 y	P
22	Chondrosarcoma	54	F	Tibia	6 y 7 m	P → G

a: years, *b*: months, *c*: Kiel bone grafted with autogeneic bone, *d*: monostotic type, *e*: polyostotic type, P: Poor, F: Fair, G: Good, E: Excellent

Table 2 Ragiological grades of the grafted Kiel bones

Excellent:	Implanted Kiel bone is completely replaced by the autogeneic new bone.
Good:	Absorption with sclerosing of the grafted bones without clear delineation of the margin of the implanted bone.
Fair:	Delayed union patterns with clear delineation of the margin of the implanted bone.
Poor:	Non-union patterns of the implanted bone retaining the marginal clear zone, or absorption of the grafted bone without bony formation.

Table 2. There are two subtypes in the radiological findings of the Poor grade (non-union type and absorption type). Both are clinically thought to be failure in bone grafting. We classified both types as Poor grade.

Results

None of the 22 cases had secondary abnormal fever, inflammation, or infection during the follow-up period.

We evaluated the radiological findings at the last follow-up (mean follow-up period; 14.8 years) (Table 3). Four lesions were classified as Excellent, 14 were Good, 2 were Fair, and 5 were Poor. Mean age of the patient at the time of the operation in the Excellent group was 5.7 years old, Good was 18.8 years old, Fair was 16.6 years old, and Poor was 11.9 years old. All lesions in the Poor group were polyostotic fibrous dysplasia.

Table 3 Bone grafted cases classified by radiological grades at final follow-up examination

	Radiological grades			
	Excellent	Good	Fair	Poor
Number of cases	4	14	2	5
Mean age at implant (years)	5.7	18.8	16.6	11.9

(Mean follow-up period, 14.8 years)

Table 4 Bone grafted cases graded by radiological examination performed at different periods after operation

	Number of cases					
	Follow-up period after operation (years)					
Grades	1	3	5	10	15	20
Excellent	0	0	0	0	2	4
Good	1	6	6	11	10	4
Fair	0	6	9	3	1	0
Poor	24	13	10	7	1	0
Total	25	25	25	21	14	8

At 1 year after the implantation, only one lesion (case 14) was classified as Good. Follow-up at 3 years showed an increase in the number of lesions in the Good group. However, 7 of 8 lesions of the polyostotic fibrous dysplasia were classified as Poor. At 3 to 5 years after grafting, there was a major difference in the rate of acceleration of improvement in each group. At 10 years, the number in the Good group had increased to 11 lesions. At 15 years, 12 of 14 lesions were identified as better than Fair. All lesions were either Excellent or Good at 20 years (Table 4).

The younger the patient, the more rapidly kiel bone grafts were incorporated into the recipient bed. Most of lesions were Excellent or Good at 10 years, excluding those of polyostotic fibrous dysplasia (Table 1). All lesions of fibrous dysplasias in Poor grade at the final follow-up were the absorption type.

Case 14. A 4-year-old male developed pain in the distal end of the right forearm after a fall. A radiolucent area with a fracture line was found in the distal metaphysis of the right radius. Curettage of the lesion and Kiel bone grafting was performed in September, 1968. The histological diagnosis was fibrous dysplasia. A radiolucent zone reappeared in the same area 4 months later (Fig. 1a). A second operation to treat the recurrent lesion was performed using the same methods as the initial operation (Fig. 1b). Incorporation of the grafted bone seemed to be good at 6 months after the second operation (Fig. 1c). The grafted bone was completely replaced by bone from the recipient bed (Fig. 1d).

Case 20. A 19-year-old woman complained of right coxalgia in March, 1974. Radiolucent lesions were found in the pelvis and both femoral necks (Fig. 2a). Kiel bone was implanted after curettage of the lesions of the right femoral neck (Fig. 2b). The histological diagnosis was polyostotic fibrous dysplasia. The grafted bone seemed to have gradually disappeared 3 years later (Fig. 2c), and coxa vara gradually progressed (Fig. 2d).

Case 22. A 54-year-old woman with chondrosarcoma. Abnormal shadow in the right tibia was seen radiologically in April, 1977 (Fig. 3a), and open biopsy histologically confirmed chondroma. Kiel bone was grafted alone after curettage of the lesion. About 3.6 years postoperatively, the grafted bone had gradually become enmeshed in the recipient bed (Fig. 3b). At 6 years, she occasionally complained of right gonalgia, and radiographs revealed periosteal reactions and a sclerosing shadow from the upper meta-

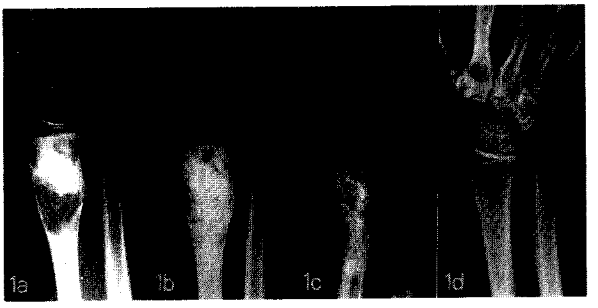

Fig. 1 Case 14 (a) Monostotic fibrous dysplasia of the distal end of the right radius in a 4-year-old boy, showing a radiolucent area 4 months after initial operation. (b) The same case, immediately after the second operation and curettage of the lesion and Kiel bone grafting. (c) Six months after the second operation, incorporation of the grafted bone was good. (d) At 20.5 years after the second operation, the grafted Kiel bone was completely replaced by bone from the recipient bed.

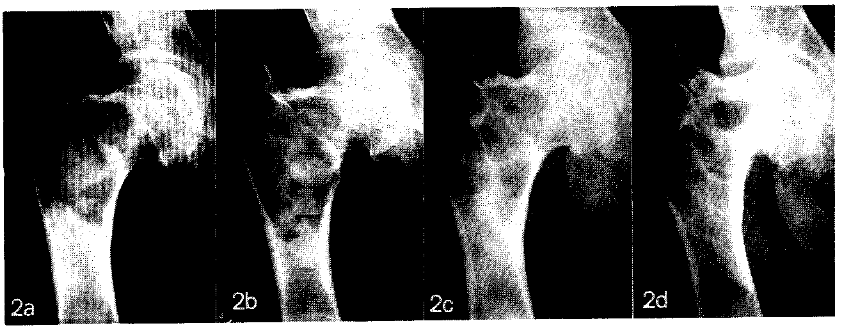

Fig. 2 Case 20. (a) Polyostotic fibrous dysplasia of both femoral necks in a 19-year-old woman. (b) The same case, immediate after curettage of the right femoral neck lesions and Kiel bone grafting. (c) At 3 years after the operation, the grafted Kiel bone appears to have gradually disappeard in the recipient bone bed. (d) At 16.2 years after the operation, the grafted bone is not visualized, and coxa vara is progressing.

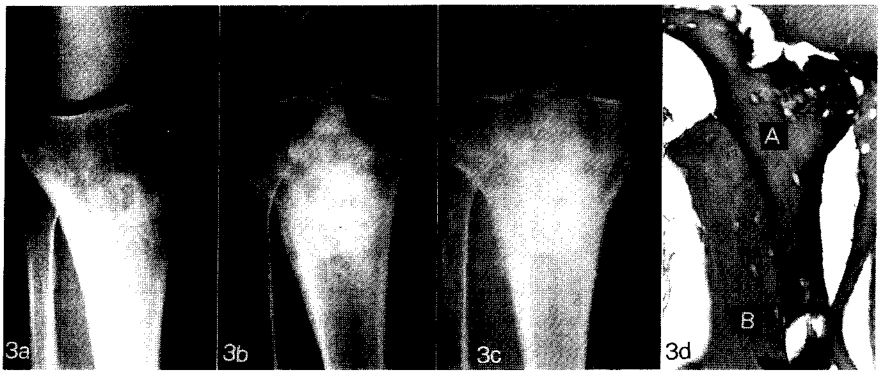

Fig. 3 Case 22. (a) Chondrosarcoma of the proximal right tibia in a 54-year-old woman with gonalgia and a sclerotic shadow in the tibia. (b) At 3.6 years after curettage of the lesion and Kiel bone grafting. the margin of the grafted bone has become obscure. (c) At 6.6 years after the operation. Periosteal reaction is seen around the lesions. (d) Histological section showing that autogeneic new bone has grown in contact with the Kiel bone without intervening fibrous tissue. A: Kiel bone. B: Autogeneic new bone.

physis to the epiphysis of the tibia (Fig. 3c). As a malignant change was suspected, above the knee amputation was performed after histological confirmation of chondrosarcoma. On the sectioned sample, autogeneic new bone had grown in contact with the kiel bone implants without interposing fibrous tissue 6.6 years after the grafting (Fig. 3d). The findings were thought to represent replacement of the implants by autogeneic bone from the recipient bed.

Discussion

We evaluated the radiological findings concerning the changing patterns of Kiel bone 5 to 22 years after implantation using the Terakado's classification of 5 grades; completely replaced type, absorption with sclerosing type, delayed union type, non-union type, and dislocated type (11). The dislocated type was not represented in our cases and was therefore deleted from further discussion in this report (Table 2). Seventy-two percent of the lesions were classified as Excellent or Good at the final follow-up. The radiological evaluation therefore confirmed satisfactory results. If polyostotic fibrous dysplasia was excluded (8 of the 25 lesions), all cases would be rated Excellent to Fair.

Based on the long-term follow-up, the results of Kiel bone grafting were better than anticipated. This seemed to be attributable to 1) an abundant blood supply in the recipient bed other than pseudoarthrosis, and 2) the age of the subjects was generally young. Vigorous absorption of the grafted bone replaced with new bone formation depends on growth age. In a recipient bed, such as the cancellous bone of infants and children, which has good osteoconductive activity, good incorporation can be expected even with Kiel bone (10). A lengthy postoperative term appears to be one of the important factors in assessing results, previous reports of Kiel bone grafts showed little utility in short follow-up periods.

Several factors for successful bone implantation include intensity, toxicity, immunologic response, and most importantly, incorporation into the recipient bed. The two most important factors determining the degree and speed of the incorporation are said to be osteoinduction and osteoconduction (8). Kiel bone has relatively little osteoconductive activity (10).

Osteoconduction depends on the presence of osteoprogenitor cells, osteoblasts, and blood supply from the recipient bed (8). If osteoconduction factors are abundant, autoclaved bone or Kiel bone can be incorporated in the recipient bed where vascular structures can invade into the grafted bone. The implants are then absorbed, and gradually substituted by new bone formation. We achieved a better graft of Kiel bone with autogeneic bone in an aged recipient bone bed which is though to be poorly osteoconductive, so the incorporation of the Kiel bone was not so delayed (case 10).

Judging from the results at our last follow-up, Kiel bone implants can be substituted for the recipients' new bone in some patients. Most of lesions were rated as Excellent or Good, within 10 years after implantation, as illustrated by the histological sections from case 22 (Fig. 3d). In 1982, McMurray noted that in the early postoperative phase, dense collagen and fibrous tissue evoked by the Kiel bone may provide temporary support to the grafted area (12). However, in time this fibrous proliferation will be the underlying cause of the eventual failure of the Kiel grafts (12). At about five years, the reactive fibrous tissue is absorbed and the Kiel bone grafts are directly in contact with autogenous new bone (Fig. 3d). Kiel bone implant seems to be contraindicated for polyostotic fibrous dysplasia, because the graft undergoes degeneration and absorption as the disease advances (cases 18 to 21).

These results suggest that Kiel bone implants can be used if good osteoconductive activity is expected in the recipient bone bed. This includes areas such as cavities resulting from the curettage of benign bone tumors.

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