Cranioplasty with Custom-made Artificial Bone after Resection of Multilobular Bone Tumor in a Dog


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Abstract: A 7-year-old spayed female Welsh corgi presented with a mass of the skull. The mass was diagnosed as multilobular bone tumor and surgically removed. To treat a large bone defect after the tumor removal, custom-made artificial bone fabricated by a 3-dimensional ink-jet printer was implanted in the defect. Follow-up computed tomography evaluation was performed for 4.3 years. The implant was well integrated with the skull and had covered the large bone defect during the follow-up period. Gradual degradation of the implant began 6 weeks after surgery. It provides an additional option for the treatment of large bone defect.

Key words: multilobular bone tumor, custom-made artificial bone, large defect, calcium phosphate, dog.

Introduction

Multilobular bone tumor is a relatively rare form of malignant bone tumor and is typically observed in the skull, maxilla, mandible, orbit, and other sites in middle-aged, large breed dogs (5,17). These tumors do not display rapid growth, but local invasion is often observed. The recurrence rate is 47-58% after tumor removal (5,15). Metastasis to distant organs, particularly to the lung, is reported in 56-58% of patients with a median time to metastasis of 420-542 days (5,15).

Surgical removal is the treatment of choice for multilobular bone tumors and is associated with an excellent prognosis when the tumor is completely removed (5,16). Although the effectiveness of chemotherapy and radiation therapy has not been proven, radiation therapy is sometimes performed for the local control or palliative treatment of the tumor (10).

Calcium phosphates, such as hydroxyapatite (HA), α-tricalcium phosphate (TCP), and β-TCP, have been widely used as artificial bone materials for various patients because of their biocompatibility and osteoconductivity. Herein, we report the development and use of a novel custom-made artificial bone made from α-TCP, fabricated using a three-dimensional (3D) printer, based on 3D data of the bone defect (8). The shape of the artificial bone was well matched with the bone defect and showed good osteoconductivity in vivo (3).

The purpose of this study was to report the efficacy of this custom-made artificial bone in a dog over 4.3 years after implantation following removal of a multilobular bone tumor of the skull.

Case

A 7-year-old spayed female Welsh corgi weighing 10.7 kg presented with a mass of the skull to the veterinary medical center of the university of Tokyo. The mass was firmly adhered to the skull at the vertex. On physical examination, the patient was otherwise in good health. The results of complete blood count and serum biochemistry were within normal ranges, and thoracic radiography revealed no abnormal findings. On computed tomography (CT), the mass, measuring 2.0 cm × 2.1 cm × 1.5 cm, appeared lobulated and extended rostrally from the vertex to the caudal margin of the frontal sinus.

Fig 1. Transverse computed tomography image of the mass.
without compression of the brain (Fig 1). Biopsy revealed the mass to be a multilobular bone tumor.

Total intravenous anesthesia using propofol was performed after administration of atropine sulfate (25 µg/kg SC). Fentanyl hydrate (5-20 µg/kg/h IV) was continuously administered during the surgery. Cefazolin (20 mg/kg IV) was administered at the time of anesthetic induction, and then every 2 h until the end of the surgery. The midline skin and subcutaneous tissue were incised and the mass exposed (Fig 2A) and then removed carefully by using a periosteal elevator and a rongeur. After removal of the mass, the margins of the defect were trimmed using a round burr with saline flushing (Fig 2B). The skin and subcutaneous tissue were sutured routinely.

Postoperatively, fentanyl hydrate (5 ug/kg/h IV) was administered overnight, and cefazolin (20 mg/kg SC) given twice daily for 3 days. The dog was discharged with cephalexin (20 mg/kg PO) to be given twice daily for 5 days.

CT was conducted to confirm the size of the bone defect after surgery, and this 3D data was used for the fabrication of the custom-made artificial bone (Fig 2C). On CT, the mass appeared to have been completely resected, and the defect size was 2.3 cm × 2.3 cm.

The fabrication process of the custom-made artificial bone was described in our previous study (8). Briefly, CT data of this patient and of the skull of a Welsh corgi with no abnormal skeletal structures were converted to CAD data and merged, allowing the CAD data of the bone defect of the patient to be extracted. The implant design was modified by the addition of 4 horizontal and 4 vertical cylindrical holes, each measuring 2 mm in diameter, to facilitate the migration of osteogenic cells and blood vessels (8). The artificial bone was fabricated from α-TCP powder by using the CAD data and a 3D ink-jet printer and was autoclaved prior to use.

Artificial bone was implanted 2 weeks after the tumor-removal surgery, and the anesthetic regime, surgical preparation, and approach were the same as those for the first surgery. The dura mater was slightly swollen and was carefully separated from surrounding tissues by using a periosteal elevator. The margins of the bone defect were prepared for implantation of the artificial bone with a rongeur. The artificial bone fitted well into the bone defect. A fibrin sealant was sprayed on to the defect to fix the artificial bone in situ (Fig 3A). The skin and subcutaneous tissue were sutured routinely. After closure of the surgical wound, CT was performed to confirm the placement of the artificial bone (Fig 3B).

During the follow-up period of 4.3 years, CT was periodically conducted (Fig 4). Bony bridging was observed between the implant and the skull from 2 months after implantation (Fig 4A). Resorption of the implant began at the superficial margins, 6 months of the implantation (Fig 4B). This degradation appeared mainly at the region of the cylindrical holes, and the implant was partially fragmented at 9 months after
implantation. A linear bony structure was observed at the region of implant degradation 2 years after implantation (black arrowhead, Fig 4A). Osteolytic changes were seen at the left and right implant margins at 9 and 20 months after implantation, respectively, and these regions gradually increased in size (white arrow, Fig 4). Four years and 4 months after implantation, there were no clinical symptoms or implant complications, and there was no evidence of recurrence of the mass or metastasis to the lung.

**Discussion**

The prognosis of multilobular bone tumor in dogs is generally good when the tumor can be removed completely (3,15). In this case, the tumor appeared to have been completely resected, and a large bone defect was created on surgery. As this defect size was too large to be repaired spontaneously, a custom-made artificial bone implant was used in order to protect the exposed dura mater and brain after the tumor removal (14).

In previous reports of similar cases, reconstructive surgery with various implants, including cortical allografts, has been described (11). However, these techniques require the preparation and trimming of stock bones from the bone bank in Japan, which can be challenging. Polymethylmethacrylate (PMMA) has also been used for cranioplasty. Molded PMMA was implanted into the defect after excision of a multilobular bone tumor and showed excellent cosmetic results and prognosis, with only minor complications (3). However, PMMA is non-absorbable and can induce tissue necrosis and infections (3).

Calcium phosphates have been widely used in human and animal clinical practice because of their excellent biocompatibility and osteoconductivity (6,12,16). Calcium phosphate cement has been used for craniofacial reconstruction in humans.

![Fig 4. Transverse computed tomography images (A) and reconstructed three-dimensional images (B) after custom-made artificial bone implantation. White arrows indicate the osteolytic regions and black arrows indicate the linear bony structure.](image-url)
Owing to its self-setting capacity and easy manufacture (7), α-TCP, the main component of the custom-made artificial bone used in this study, has been used as an injectable calcium phosphate cement and has shown remarkable mechanical strength and biological behavior (9,13).

Since the custom-made artificial bones were fabricated based on CT data of the bone defect, they matched well to the shape of the defect and could be easily implanted into the defect site (8). These characteristics make this type of implant particularly suitable for use in bone defects with complicated shapes, such as those in the skull or face. Furthermore, as demonstrated here, custom-made implants facilitate surgery and can reduce implant manipulation time for surgeons. The implant was integrated to the skull from 2 months after implantation and could protect the dura mater and brain successfully during the follow-up period of approximately 1560 days.

The degradation of the implant may occur through osteoclastic phagocytosis, and the release of calcium phosphates into the extracellular fluid. In this case, degradation of the implanted custom-made artificial bone started 6 months after implantation. The degradation occurred at the peripheral region of the implant, and gradually progressed to the central area during the follow-up period. As osteolytic changes of the skull were observed on CT, it is possible that the degradation was related to the neighboring osteolytic change. However, the degradation of the implant started before the osteolytic region was clearly formed (9 months after the implantation), suggesting that these processes occurred independently. This finding is supported by the appearance of the osteoclasts at the surface of the implant, which we reported in our previous study (8). The results of our 4.3-year follow-up period demonstrate that complete degradation of the implant occurs slowly enough for it to be covered by the host regenerated bone.

On CT at 2 years after implantation and thereafter, a linear structure was seen after the degradation of the implant (Fig 4, black arrowhead). This linear structure seemed to be the ingrowth of new bone tissue at the sites of the 4 horizontal cylindrical holes, which had been incorporated into the implant body for this purpose (4,8). New bone formation within the cylindrical holes may contribute to the covering of the defect at an earlier time than if no holes were present.

The cause of the osteolysis of the skull was unclear. It has been reported that foreign body reactions with osteolytic changes could occur with the use of absorbable polymer implants (1). However, these changes are temporary and do not induce permanent tissue damage in humans (1,2). To our knowledge, there has been no report of osteolytic change with calcium phosphate implants. In this case, owing to the fact that the osteolytic regions gradually increased, the potential recurrence of the tumor should be considered. However, as the patient was in good health 4 years after surgery, with no abnormal findings on clinical examination, the owner did not agree to biopsy for further investigation of the osteolytic changes.

In conclusion, the implantation of custom-made artificial bone made from α-TCP could be an effective treatment modality for large bone defects of the skull after removal of multilobular bone tumor. The dog remained healthy with no evidence of metastasis during the follow-up period of 4.3 years. The implant covered the defect successfully and was gradually degraded without side effects.

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References


개의 다엽성 골종양 제거후 커스텀 메이드 인공뼈를 이용한 두개골성형술

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요 약: 두개골의 종괴를 가진 7세 암컷 펭귄기가 내원하였다. 종괴는 다엽성 골종양으로 진단되었으며, 외과적으로 제거하였다. 종괴 제거후 발생한 대형 골결손부를 치료하기 위해 3D 잉크젯 프린터로 제작한 커스텀 메이드 인공뼈를 결손부에 이식하였다. 이식 후 3년여동안 CT촬영을 통해 변동을 관찰하였다. 인공뼈는 관찰기간동안 주전 두개골과 성공적으로 융합되어 결손부를 수복하고 있었으며, 이식후 6개월부터 점차적인 인공뼈의 흡수상이 확인되었다. 커스텀 메이드 인공뼈가 대형 골결손부의 또 다른 치료방법으로서 사용될 수 있을 것이라고 기대된다.

주요어: 다엽성 골종양, 커스텀 메이드 인공뼈, 대형 골결손부, 인산칼슘, 개