Resorption of synthetic porous hydroxyapatite and replacement by newly formed bone

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Abstract Synthetic porous hydroxyapatite (HA) is commonly used as a bone substitute for bone defects which, previously, would have been treated by autogenous bone grafting. HA has been thought to be a nonbiodegradable material that remains as it is implanted. However, after long-term follow-up, some authors report that the margin of implanted HA blocks or granules is absorbed, suggesting that HA is biodegradable. We experienced a patient in whom synthetic HA blocks implanted in a bone defect of the ilium after the harvesting of full-thickness bone for grafting were extensively absorbed and replaced by newly formed bone 6 years and 7 months after the implantation. Therefore, we conclude that HA is biodegradable. Sintering temperature, porosity, and pore diameter seem to influence the biodegradability of HA.

Key words Hydroxyapatite · Biodegradability · Bioresorption

Introduction

Surgery for bone tumors or trauma sometimes results in serious huge bone defects that have to be repaired. Conventionally, such bone defects have been treated by autogenous bone grafting, usually from the ilium. However, autogenous bone harvested from the ilium is limited in volume, particularly in patients with re-grafting or in younger patients. The advent of ceramics as a bone substitute has been epoch-making for these patients. Large numbers of basic and clinical studies of such ceramics have been published by many authors. Commercially available ceramics that are used as a bone substitute are hydroxyapatite (HA) and tricalcium phosphate (TCP), with HA probably being used more frequently. Therefore, it is of great importance to understand the biological behavior, i.e., the biodegradation, of HA in the human body. HA has been thought to be a nonbiodegradable material that remains as it is implanted. However, after long-term follow-up, some investigators have reported that the margin of implanted HA was absorbed. We experienced a patient in whom synthetic HA blocks implanted in a bone defect of the ilium had almost disappeared, and were replaced by newly formed bone, on plain radiographs. We present the case and review the literature regarding the biodegradation of HA.

Case report

A 20-year-old man had giant-cell tumor of bone in the distal epiphyseal-metaphyseal region of the right femur. He had no remarkable past or family history. Plain radiographs showed an osteolytic lesion with a diameter of 7 cm at the distal end of the right femur. Surgery, i.e., curettage followed by cryosurgery, was performed. The subsequent huge bone defect was filled with autogenous morselized bone chips made of full-thickness bone harvested from the ipsilateral iliac crest. We implanted three blocks of synthetic porous HA (sintered at 900°C) (Bonfil; Mitsubishi Material, Tokyo, Japan) into the bone defect, which measured 8 × 3 cm, in the iliac crest. The size of each block was 4 × 3 × 1 cm, with porosity of 70% and mean pore diameter of 280 µm. One block was placed as a block, and the two remaining blocks were crushed into several pieces to fill the remaining defect. No complication occurred after the surgery. There was no inflammation in the iliac region after the wound had healed. No allergic reaction or toxicity was seen by routine blood examinations. There were no clinical symptoms, e.g., pain or discomfort, in the iliac region during the follow-up period. Plain radiographs of the ilium were taken periodically. Plain radiographs taken 7 months after the surgery showed no radiolucent
zone around the HA, which suggested that the HA was well incorporated with newly formed bone around it (Fig. 1a). Three years and 4 months after the surgery, the HA block had become smaller, and the margin of the HA was obscure, suggesting that biodegradation of the HA surface had occurred (Fig. 1b). Bioresorption of HA was apparent. Six years and 7 months after the surgery, the HA had almost disappeared and had been replaced by newly formed bone (Fig. 1c).

Discussion

Hydroxyapatite (HA) is widely used as a bone substitute to fill bone defects. It is biocompatible, easily fabricated into any size or shape, and offers a chemical environment and surface conducive to new bone formation.\textsuperscript{1,7} Its clinical usefulness has been reported by many authors.\textsuperscript{6,11,15-17,21} Desirable features of bone substitutes are that: (1) they are nontoxic and do not cause allergic reaction or inflammation, (2) they are mechanically strong, (3) they have osteoinductivity or osteoconductivity, and (4) they are biodegradable and replaced by newly formed bone. Commercially available ceramics for bone substitutes are hydroxyapatite (HA) and tricalcium phosphate (TCP). TCP is biodegradable and is replaced by bone.\textsuperscript{1,2,7,10,13,14} Because it is brittle and its half-life is short, it is rarely used at sites where mechanical strength is required.\textsuperscript{1} The biodegradability of HA is, in contrast, controversial. Previously, HA was thought to be nonbiodegradable, because no resorption could be detected in animal experiments.\textsuperscript{1,4,5,8,13} Although biodegradability was not apparent, some investigators observed, in their histological studies, that osteoclast-like multinucleated giant cells were biodegrading HA.\textsuperscript{3} However, the biodegradability of HA has been proven in both basic research\textsuperscript{12,14,18-20} and in clinical studies.\textsuperscript{6,15,17,21} The mechanism of implant resorption is still not completely understood. It is assumed that HA is degraded either by simple dissolution or by cell-mediated processes (osteoclastic phagocytosis).\textsuperscript{1,7} Because HA is practically insoluble in water,\textsuperscript{13} the latter, cellular, mechanism would seem to be much more important than simple dissolution. In the basic research studies, various types of HA blocks were implanted into the femurs or tibias in rats,\textsuperscript{18-20} rabbits,\textsuperscript{7} and dogs,\textsuperscript{3} demonstrating volume loss of the implants, in addition to proving that osteoclast-like multinucleated giant cells or macrophages biodegraded the HA blocks. Clinical studies, on the other hand, demonstrated that, in radiographs taken more than 5 years after the implantation of HA blocks, the margins of the implanted HA blocks were resorbed. However, extensive resorption of HA observed radiographically has not yet been reported.

We did not perform either computed tomography (CT) examinations or biopsy to evaluate the bioresorption of HA. Even with CT, it would be difficult to precisely assess the bioresorption of HA, because the trabeculae of porous HA are indistinguishable from

\textbf{Fig. 1a–c.} Plain radiographs of the right ilium after the implantation of hydroxyapatite (HA) blocks. \textbf{a} Seven months after the implantation surgery. There was no radiolucent zone around the HA. \textbf{b} Three years and 4 months after the surgery. The size of the HA was smaller and the margin of the HA was more obscure than these findings shown in \textbf{a}. \textbf{c} Six years and 7 months after the surgery. HA had been resorbed and replaced by newly formed bone.