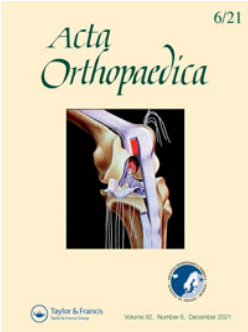

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Case report: Remodeling of the tibia after grafting of a large cavity with particulate bioactive glass-hydroxylapatiteon treatment of fibrous dysplasia with 13 years' follow-up

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Remodeling of the tibia after grafting of a large cavity with particulate bioactive glass-hydroxylapatite—case report on treatment of fibrous dysplasia with 13 years' follow-up

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A 28-year-old woman had had pain in her right tibia during outdoor leisure-time activities for 1 year. A slight expansion in the middle of the bone was palpated. She was 177 cm tall, weighed 64 kg and had normal skin. Radiographs showed a large cystic lesion, which had a cortex that was only 2–3 mm thick (Figure 1a). CT and MRI revealed an abnormal mass in the tibia. Open surgical biopsy showed fibrous dysplasia.

The patient, a dentist, was told that we might fill the cavity with autogenous bone and artificial biomaterials—a mixture of glass-hydroxylapatite—and she agreed to undergo this treatment. The cavity was opened by sawing two rectangular

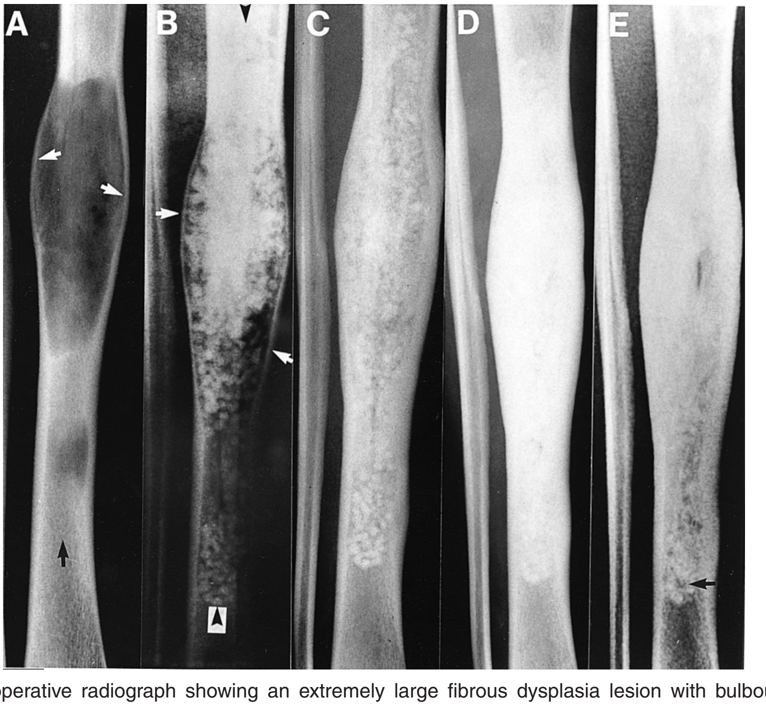


Figure 1. a. Preoperative radiograph showing an extremely large fibrous dysplasia lesion with bulbous contour and marked thinning of the cortex (white arrows). The lowest part of the lesion extends into the distal tibia (black arrow).
b. Postoperative radiograph after curettage showing the defect, which had a very thin cortex (white arrows) and was filled with a mixture of bioactive glass and hydroxylapatite composite granules. Note the lesion extended more distally and proximally (black arrow heads) than was expected looking at the preoperative radiograph (1a). The cavity now contained biomaterial that extended two thirds of the length of the tibia.
c. The radiograph 6 months later shows thickening of the cortical new bone. Some of the granules have rounded borders.
d. Thickening of the cortex during remodeling has increased at 3 years and 4 months after the grafting operation.
e. Radiograph after 13 years shows further cortical thickening and remodeling of the tibia. A small oval defect, caused by the trepanation operation and the biopsy, is seen. Remnants of degrading biomaterial granules are visible in the distal tibia (arrow).

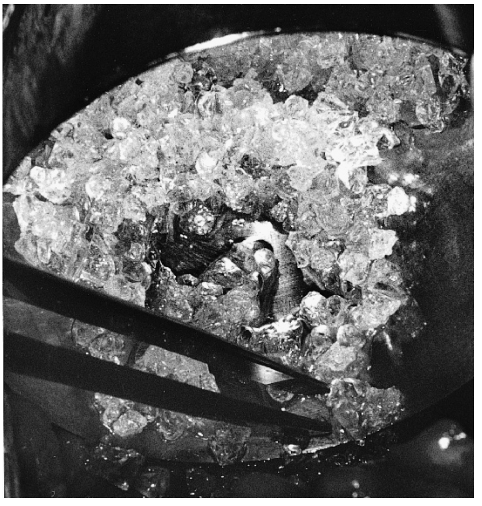


Figure 2. Particulate bioactive glass granules in a container moistened with distilled water.

windows in the anterior cortex. The tumor was removed by curettage and the cavity drilled and smoothed with a rose trepan and washed with saline (March 1987). The cavity measured 20 cm in length and 2–4 cm in width, which was larger than that seen on in the radiograph (Figure 1b); it therefore entailed a risk of pathological fracture. It was filled with a mixture of bioactive glass (GL-3), a glass/hydroxylapatite (dense) composite (HGL) and autogenous bone chips taken from the iliac crest. The glass, GL-3, consisted of granules 1–6 mm in diameter and particles of powder ranging in size from 40–150 μm (Figure 2). Its chemical composition as a percentage of weight was: SiO_2 52.9%, Na_2O 25.8%, CaO 10.7%, P_2O_5 5.4%, Al_2O_3 2.0%, and B_2O_3 3.2%. The composite (HGL) was prepared by melting a glass GL-3-hydroxylapatite mixture 50:50 for 5 min at 860 °C. The HA granules was between 45 and 100 μm. The percentages of the biomaterials used for the filling were: GL-3 50, HGL 40, and autogenous 10. Therefore, the percentage of bioactive glass was 70 from the graft material, which was sterilized by autoclaving at 180 °C. After filling, the cavity was covered with the cortical lids sawed from the anterior tibia, and the wound was drained and closed. A plaster cast was used for 6 weeks and weight bearing was gradually increased.

Follow-up

The patient has been followed for more than 13 years and the clinical course was uneventful during the first 3 years. However, at 3 years and 4 months, she developed a slow, silent, and small infected sinus. Bacterial cultures showed growth of *Staphylococcus epidermidis*. The sinus was treated by debridement, and removal of some thickened tissue from the cavity. Thereafter, the wound healed and the patient did well and has continued working as a dentist.

The incorporation of the filling material was evaluated by plain radiographs, isotope scans (including CT SPECT imaging), and CT. Biopsies for histology were taken 3 years after filling the cavity, during the debridement operation, and 13 years later for scientific purposes. Van Gieson and hematoxylin-eosin stains were used for the sections of decalcified specimens.

Results

Radiographs and CT showed that the markedly thinned cortex began to thicken 6 months after grafting (Figure 1c). The remodeling and bone healing continued to increase during the follow-up (Figures 1d,e). The cortex became even thicker than that in the healthy left tibia, and the medullary part narrowed, as also shown on the CT illustrations (Figures 3a, b, c, d, the healthy left tibia). In the medullary cavity, structural changes were seen after 13 years (Figure 3c), which indicated the formation of intramedullary bone/connective tissue, as found in the biopsy (Figure 5c). Scintigraphy ^{99m}Tc-DPD (^{99m}Tc dicarboxypropane diphosphonate) and SPECT (Single Photon Emission Computer Tomography) showed that the cortical tracer uptake at 1 month after filling was higher than that in the bone marrow (Figure 4a). The uptake increased during the following 1–3 years, which indicated an increase in mineral metabolism, and later also in the marrow (Figures 4b-d).

Degradation of the Glass 3 granules, new bone tissue in contact with the biomaterial and connective tissue with some histiocytes were seen in the histological sections at 3 years (Figures 5a,b). Hydroxylapatite structure could no longer be distinguished. Biopsies taken at 13 years from the medullary canal showed bone and connective tissue, but no biomaterial could be seen (Figure 5c).

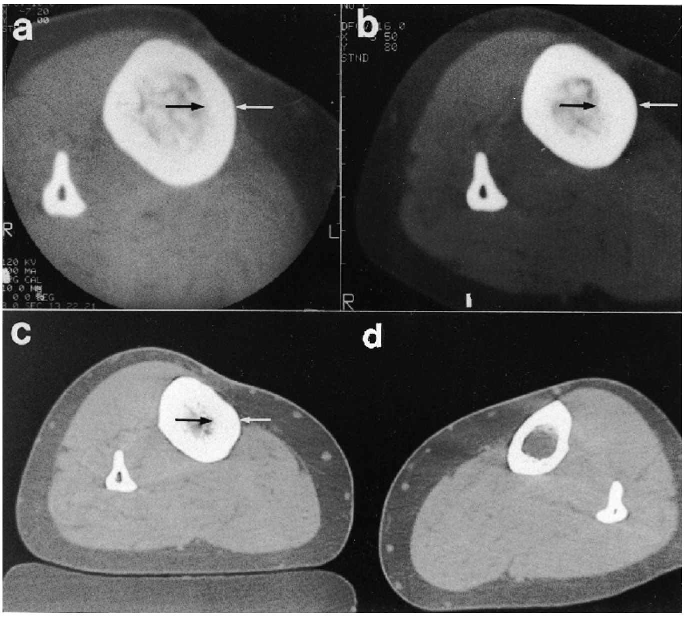


Figure 3. CT illustrations.
a. A transverse CT scan 1.5 years after surgery.
b. 3 years and 4 months after surgery.
c. 13 years after the operation, the cortex (arrows) has become thicker than that of the healthy left tibia (3d).
The medullary canal is narrower and contains half dense tissue material as compared to the healthy left tibia (3d).

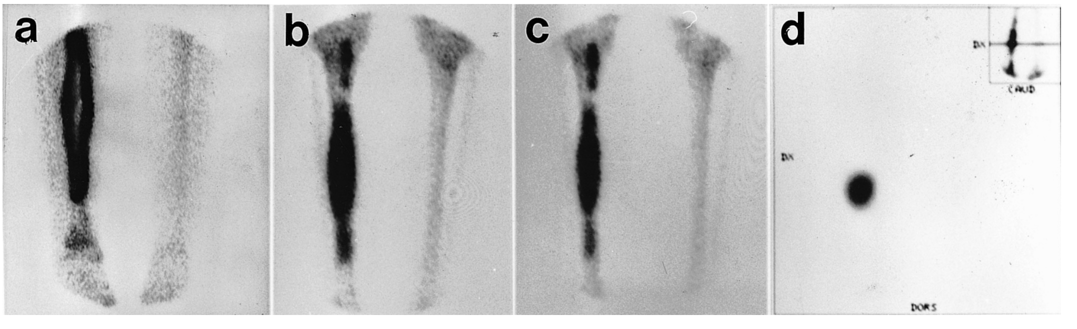


Figure 4. Scintigraphy. At 1 month after surgery (a), tracer uptake is very high in the cortex. In the later images (b and c), this uptake can also be seen in the marrow. The transaxial tomographic slice (SPECT) at 2 years 8 months after surgery (d), shows a homogeneous tracer uptake throughout the marrow.

Discussion

To our knowledge, this is the first and largest bone cavity treated with bioactive glass grafting. In 1987, clinical experience concerning the treatment of large bone defects using glass was scanty—only the data on maxillofacial surgery had been reported (Wilson et al. 1994). During recent decades, many types of bioactive glass of various compositions have been tested. Before our patient was operated on, many chemical (Karlsson et al. 1989, Andersson et al. 1990) and experimental studies in animals (Kangasniemi and Yli-Urpo 1990, Aho et al. 1993, Suominen et al. 1995) had investigated the incorporation of glass into bone. We chose hydroxylapatite as the second component of the bone substitute mixture because in the late 1980s, there were some clinical reports of patients who had been treated with it (Buchholz et al. 1989, Loty et al. 1990, Uchida et al. 1990). Moreover, in the 1960s, we had had some clinical success, using heterogeneous anorganic bone (Ossar) (Viikari and Aho 1963), which chemically resembles hydroxylapatite.

The noninvasive radiological methods for assessing bone healing, SPECT and CT, showed an increase in the rate of mineral metabolism in the medulla and remodeling of the cortical bone which resulted in a tight homogeneous cortex, which looked strong. It seems very unlikely that the cor-

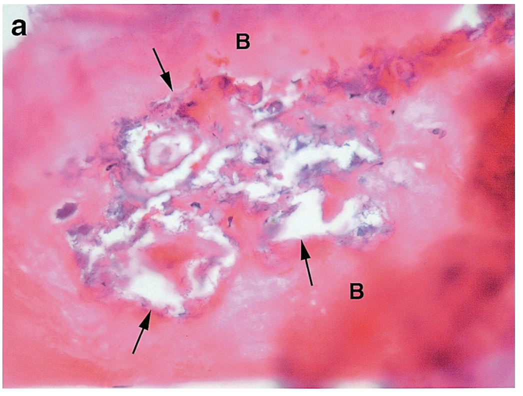
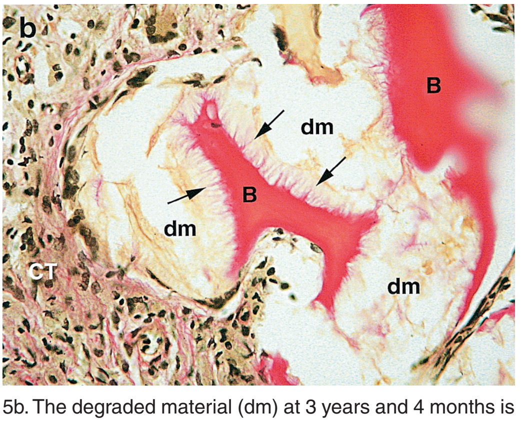
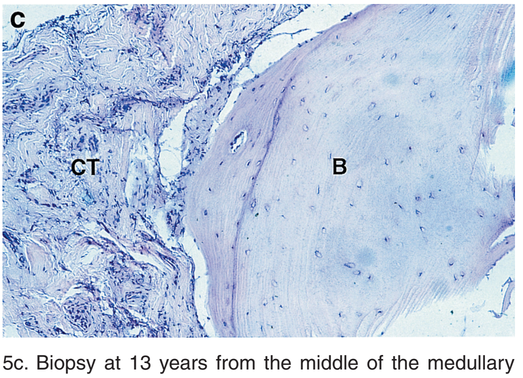


Figure 5a. At 3 years and 4 months after surgery, subtotal degradation of the bioactive glass-hydroxylapatite material has occurred. The shape and the borders of the granules can no longer be distinguished. The bone (B) now surrounds and shows tight bonding (arrows) to the degrading granular material in the middle of the picture. x390, van Gieson stain.



5b. The degraded material (dm) at 3 years and 4 months is surrounded by bone (B) and connective tissue (CT), with a few histiocytes. Some remnants of degrading glass granules with fringe-like thin lines lie side-by-side (arrows) in contact with bone (B), x400. x180, van Gieson stain.



5c. Biopsy at 13 years from the middle of the medullary cavity shows bone (B) and connective tissue (CT). The biomaterial has disappeared from the biopsy site. x150, hematoxylin-eosin.

tical thickening and remodeling could have been caused by irritation from a low grade infection of brief duration in the medullary canal. The infection was mild, and involved a small area in the cavity and the cortical thickening was seen 2 years before the infection developed. Of course, one explanation of the cortical thickening may be related to the well-known Wolff's law. However, the cortical thickening was visible already on radiographs taken at 3 months.

There are only a few histological reports on how long biomaterials remain in the human skeleton before dissolution. Some animal studies show that degradation and physiological removal of bioactive glass in bone tissue may take 6 months to more than 1 year (Heikkilä et al. 1995, Cancian et al. 1999). The silicon component of bioactive glass has been shown to be excreted safely in rabbit urine over a period of 5–6 months (Lai et al. 2001). Our case who had a large amount, 70 vol% of particulate bioactive glass in a large bone cavity, showed substantial histological degradation at 3 years, and after 13 years, no more material was seen in the biopsies. However, some remnants may be visible on the radiograph of the distal tibia (Figure 1e). Similar results have been reported by Aitasalo et al. (2001), who found glass granulae remnants after obliteration of the frontal sinus in a human 9 years after operation. The other component of the mixture which we used, dense hydroxylapatite granules, is said to begin to degrade slowly after about 6 months with a mild inflammatory cell reaction (Cancian et al. 1999). Final integration seems to take a long time, because undegraded particles of pure crystalline HA have been found 10 years after implantation in the human maxilla (Gatti et al. 2001). In conclusion, we successfully used a particulate mixture consisting mainly of bioactive glass composite to fill a large cavity in the tibia. This was one of the main reasons why bone healing occurred with incorporation of this biomaterial and very abundant cortical remodeling of the tibia.

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No competing interests declared.

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