

DEVELOPMENT OF HYBRID TYPE ARTIFICIAL BONE MARROW MADE OF HYDROXYAPATITE CHAMBER

Katsunari NISHIHARA*, Tsuyoshi TANGE**, Kazushi HIROTA*** Yasuhiko HIRAYAMA**** and Akira YANAI*****

Department of Oral Surgery, Faculty of Medicine, University of Tokyo *

Department of Pathology, Faculty of Medicine, University of Tokyo **

National Institute for Research in Inorganic Materials ***

Division of New Ceramics, Asahi Optical Company *****

Department of Plastic Surgery, Faculty of Medicine, Juntendo University *****

INTRODUCTION

Artificial inducement of bone marrow tissue with hemopoietic inductive microenvironment (HIM) in sintered hydroxyapatite (HA) chamber in vivo was carried out. This research is important to disclose mechanisms of hemopoiesis. From a phylogenic standpoint, it is known that HIM definitely existed in the organ nearest the digestive tract, i.e., spleen, in an early stage of evolution. In the second revolution of vertebrates, the internal skeleton changed into bone tissue from cartilage. From this fact of phylogenesis, we should be able to induce hemopoietic nests in a HA chamber in place of bone, if we can find optimal structural conditions. For a preliminary experiment, sintered porous hydroxyapatite plates were implanted into rib bone marrow of dogs 1). Then tissue reaction around the implanted hydroxyapatite was observed. Thereafter, we tried to induce artificially a hematopoietic field in muscles using sintered porous tubular hydroxyapatite and a new type HA plate made by a high-pressure gas technique. Then, we developed an artificial bone marrow chamber made of sintered HA, which was connected to the iliac artery of a dog. Distinct resorption of hydroxyapatite porous plates was observed in rib bone marrow without marked tissue reaction. Not only in the pore sites of tubular HA artificial bone but at the surface of the new type HA plate implanted in the dorsal muscles, differentiation of bone marrow cell clusters of the hematopoietic field

could be observed. The implanted artificial bone marrow chamber was also examined histopathologically.

MATERIALS AND METHODS

1. Apatite porous plates (5mm x 1.8mm with 20% porosity) were implanted in rib bone marrow just below the rib cartilage.
2. Tubular apatite artificial bone (20% porosity) was implanted in the femur of a 30kg adult dog.
3. Tubular artificial bone with hydroxyapatite granules and hydroxyapatite plates made by high pressure gas technique were implanted in dorsal muscles.
4. A newly developed hydroxyapatite artificial bone marrow chamber was connected to the iliac artery and recovered two months postop. Specimens for light microscopy were made and examined.

RESULTS

From these experiments, the following results were obtained:

1. In bone marrow of the rib, the sintered apatite plates dissolved and changed drastically in appearance microscopically after 12 months of implantation. Marked cartilage proliferation was observed compared to the control. The apatite was surrounded by calcified tissue. The bone marrow showed no difference from normal rib marrow. The apatite plates in the outer surface of the rib cartilage showed no marked change microscopically.

The 1st Far-Eastern Symposium on Biomedical Materials
October 6-8, 1993, Beijing, P. R. China

2. In tubular apatite bone in a femur, bone marrow formation was observed by TEM. (Fig. 1).

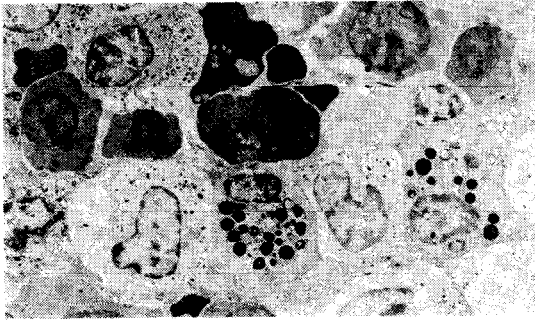


Fig. 1

3. The hemopoietic field was observed histologically around hydroxyapatite plate made by high pressure gas technique (Fig. 2).

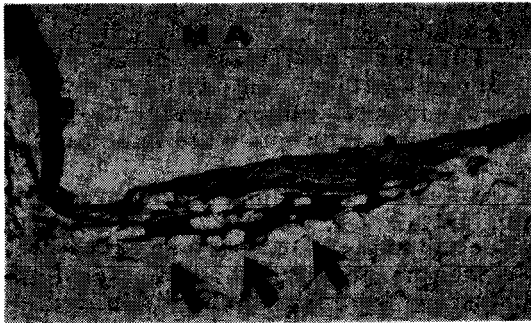


Fig. 2

4. Hydroxyapatite chamber was connected with an iliac artery and 2 months after was extirpated at the site of afferent and efferent ends of the artery. The current of the artery could be observed between the chamber ends.

DISCUSSION AND CONCLUSION

Preliminary experiments were carried out using human dental pulps. The crown part of the pulps were removed and the chambers were filled with HA granules. Several months postop, teeth were removed and specimens were examined. In the pulp chamber, calcified tissue with vessels regenerated. The mesenchymal

cells adjacent to the coagulum were assumed to differentiate to form granulation tissue with capillaries in the same way as observed in injury-healing processes. Later, from mesenchymal cells in the granulation tissue, cellular calcified tissue was assumed to be derived in the atmosphere of dental pulp surrounded by dentine. Through these healing processes, blood vessels remained in the calcified tissues. From these experiments, it was ascertained that some tissues could be regenerated around apatite granules in a chamber made of calcified substance. Therefore, we assumed that it was possible to derive bone marrow in tubular apatite artificial bone. In this atmosphere in dental pulp, apatite granules induced calcification from the mesenchymal cells. On the contrary, porous apatite plates in rib bone marrow were observed to dissolve and change in appearance with marked rib cartilage proliferation. The atmospheres in rib bone marrow and dental pulp are assumed to be quite different. Although it has been reported that growth of bone marrow cells on porous ceramics can occur in vitro, there is no report concerning bone marrow induction in ceramics chamber in vivo. In tubular apatite artificial bone filled with coagulum, bone marrow could be derived with trabeculae. From these findings, it is assumed possible to develop bone marrow in an artificial bone chamber made of apatite which is connected to an artery. We found that the apatite chamber can be utilized for an artificial organ in vivo, in which specifically differentiated organ cells can be cultured.

This work was supported by Grant-in-aid from the Ministry of Education of Japan (03557107).

REFERENCE

- 1) K. Nishihara, T. Tange, H. Tokumaru, A. Yanai and Y. Hirayama: Study on developing artificial bone marrow made of sintered hydroxyapatite chamber. *Bioceramics* 5: 131-138, 1992.