Foreign body multinuclear giant cells revisited - cellular reaction on the implantation of degradable biomaterials

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Introduction: Before clinical use all new bone substitute materials have to be validated for their long-term biocompatibility in bone. Important markers for biocompatibility and inflammatory responses are the cell types appearing after the implantation of foreign material. There, especially the role of foreign body giant cells (FBGC) is discussed controversial in the pertinent literature, such that it is not clear whether their presence marks an incompatibility of the biomaterial, or whether it belongs to a normal degradation behavior of modern, resorbable biomaterials. The aim of this study was to find correlations between the presence of FBGC and other cell types (macrophages, lymphocytes, and plasmacells) in view of biocompatibility issues as a response to different degradable bone substitutes commonly used in clinics or research settings.

Materials and methods: 33 different resorbable bone substitutes consisting of calciumphosphat, calciumsulfate, hydrogel and silk have been tested for their biocompatibility in a sheep model and were considered biocompatible and suitable for new bone formation. The materials were implanted in drillholes of 8 mm diameter and 13 mm depth within the proximal and distal femur and humerus. 6 to 8 weeks after implantation the animals were sacrificed and the bones harvested. All animal experiments were carried out according to the Swiss Laws of animal welfare and were approved by the Ethics Commission of the official veterinary authorities.

After fixation with formaline, bone blocks were cut and embedded in PMMA. Thin sections (5µm) were cut and stained with von Kossa/McNeal or toluidine blue. Semi-quantitative evaluation of samples was performed with a light microscope (40 magnif.), where cellular reactions were assessed based on a semi-quantitative score specifically developed for this individual study. Four zones representing central and peripheral zones of the original drill holes were evaluated twice and percentage (lymphocytes, plasmacells), or actual numbers (macrophages, FBGC) of cells were counted/power field (Fig. 1).

Results: 200 sections were evaluated. Degradation of biomaterials always took place from the periphery to the center in a material specific matter. New bone formation occurred parallel to the degradation of the materials. In locations with fast resorbable material, cells were found in the center of the drill holes, while with more slowly degradable materials cells were predominantly found in the periphery. Ingested materials were found in macrophages and FBGC for all materials. However, in calcium phosphate based materials, macrophages were more prominent, compared to hydrogels and silk based materials where numerous FBGC were demonstrated (Fig.2). Mostly macrophages and FBGC were alone and directly adjacent to newly formed bone, located in the so called resorption zone. However, in ca. 10% of the sections (predominantly those with the silk biomaterial) a fibrous capsule surrounding the material was discovered. This phenomenon was always correlated with a major accumulation of lymphocytes, plasmacells and multinuclear giant cells. There, bone formation was not directly parallel to the materials degradation, but followed the more distant when the inflammatory capsule formation gradually subsided.

Discussion: In the majority of the evaluated materials macrophages and FBGC were responsible for material degradation. If present alone, they were closely associated with new bone formation, thus, their presence was not considered a negative sign regarding biocompatibility issues. However, if macrophages and FBGC were associated with the appearance of high percentages of lymphocytes (cluster formation) mostly in conjunction with the formation of a fibrous capsule, bone formation seemed more inhibited and in those cases the material was judged as less biocompatible.

In conclusion it can be said that the presence of macrophages and FBGC cells alone may be a sign of the normal degradation behaviour in view of modern degradable biomaterials, whereas the formation of a fibrous capsule in combination with clusters of lymphocytes and plasma cells indicate a subclinical, but still defense reaction against the implanted biomaterial.

Fig.1: Evaluation zones within section

Fig.2: Appearance of FBC according to zone and materials