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EXPERIMENTAL STUDY ON THE INFLAMMATORY CELL RESPONSE TO XENOGENIC PORCINE DERMAL COLLAGEN IMPLANT IN MICE

Hypothesis / aims of study

The type of inflammatory response to implants, used for repair of fascial defects, influences functional outcome of surgery and the incidence and nature of local side effects. The ideal implant should be such that it induces a minimal inflammatory response but without compromising durability. We showed in rats that Pelvicol, a cell-free, cross linked porcine dermal collagen implants (Pelvicol; CR Bard), induces a lesser inflammatory response as compared to synthetic implants such as Prolene (Johnson & Johnson). In the present study we investigated in detail the characteristics of the inflammatory response induced by Pelvicol in the early post-implantation period (7d) using a mouse model.

Study design, materials and methods

Eight C57/B6 mice were subcutaneously implanted with 1 cm ^{2} of Pelvicol. At day 7 animals were sacrificed and the implant and surrounding host tissue, further called the explant, were immediately harvested. Four explants were fixed for routine histopathology, and snap frozen for immunohistochemistry (IHC). The following rat anti-mouse monoclonal antibodies were used: anti-CD3, (BD Inc.), NK-1.1 (BD Inc.), anti-neutrophils (Serotec Ltd.) and F4/80 (Serotec Ltd.) to identify T cells, NK cells, granulocytes and macrophages respectively. The other four explants were digested with collagenase, and single cells were isolated for flow cytometry analysis. Fluorescence (PE)-conjugated rat anti-mouse antibodies such as anti-CD3 (BD Inc.), NK-1.1 (BD Inc.), anti-neutrophils (Serotec Ltd.) and F4/80 (Serotec Ltd.) were used to identify T cells, NK cells, granulocytes and macrophages respectively. Samples incubated with antibodies for 30 min at 4°C. The final volume was adjusted to 500 µl and analyzed by flowcytometry (FACSort - BD Inc.). Ten thousand events were counted. Results were expressed as the mean channel fluorescence. To exclude T and B cell participation, identical experiments were performed in nude mice (who are T cell deficient) and SCID mice (who are T and B cell deficient).

Results and Interpretation of results

On histopathological study, the inflammatory response at the site of Pelvicol implantation was similar in all groups (euthymic, nude and SCID mice) at day 7. Pelvicol provoked a mild inflammatory response, consisting of mainly mononuclear cells and polymorphonuclrae cells.
Immunohistochemistry evaluation showed that the inflammatory cell populations were composed of predominantly F4/80$^+$ macrophages and granulocytes. NK-1.1$^+$ NK cells were detected, but to a less extent. CD3$^+$ T-cells were essentially undetectable. No difference was found among the groups of euthymic, nude and SCID mice.
Flow cytometry (Fig.1 & 2) revealed that macrophages/monocytes were the predominant cell type in the inflammatory infiltrate. In euthymic mice cell populations were 4.6 (0.6) % of NK cells, virtually no T-cells (1.5(0.3)%), 22.9 (2.9)% of granulocytes and 48.0(4.7)% of macrophages/monocytes. A similar profile of the percentages of these cell populations was seen in nude (T-cell deficient) and SCID (T- and B-cell deficient) mice, with one exception for NK cells in SCID mice.

Concluding message

These data suggest that Pelvicol induces a mild inflammatory response in mice, and that macrophages play a predominant role in this inflammatory process. This was confirmed in a nude and SCID mice model.

Fig.1 Flow cytometry profiles of infiltrate cell populations in euthymic, nude and SCID mice 7 days post implantation.

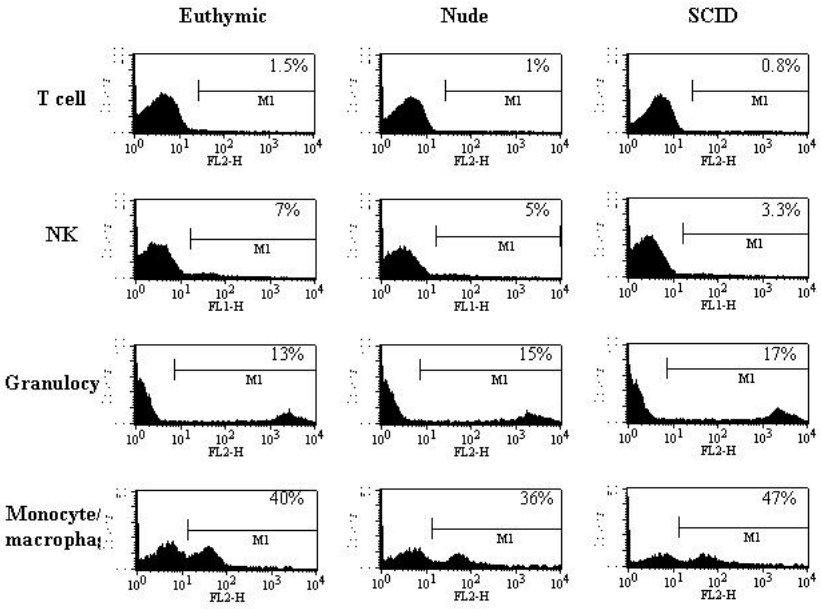

Fig.2 Summary of flow cytometry results, the mean percentage of infiltrate cells in explants in euthymic, nude and SCID mice 7 days post implantation.