Adjuvant-like Activity of Silicone Breast Implants against Extracellular Matrix Molecules

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Statement of Purpose: The issue of whether silicone breast implants are safe or not is still unresolved. A typical implant consists of an external shell of highly crosslinked siloxane polymer with amorphous silica filler, and an inner part of either saline or linear poly-dimethylsiloxane (PDMS) gel. It has been suggested that the implant surface may function as an adjuvant, causing adherent native self macromolecules to become immunogenic, and ultimately causing local autoimmune reactions with systemic complications. Thus, this study was conducted to examine the adjuvant activity of silicone shells and to elucidate the identities of immunogenic adsorbed proteins.

Methods: Glycine buffer protein extracts from 6 random recovered silicone breast implants were neutralized and separated from insoluble materials. Contaminating human immunoglobulin (Ig) molecules were removed via immobilized Protein L column chromatography. The diluted proteins in the flowthrough were concentrated and quantified. The filtrates were subsequently analyzed in SDS-PAGE and transferred onto a nitrocellulose membrane. Western blot assays were performed using sera (A to F) from the same patients where the implants were obtained. Human collagen type I (HC1) and human serum albumin (HSA) proteins were also separated and tested for reaction to the patients' sera. Additionally, sera from children with malfunctioned silicone-based ventriculo-peritoneal (VP) shunts[1] were utilized as 1° Ab for hybridization to the protein extracts. ELISA was conducted using the glycine extracts as coating antigens. To characterize the possible target of reactive patient sera, HC1, human collagen type III (HC3), as well as HSA and fibronectin (FN) were also used as coating Ag for ELISA.

Results and Discussion: Several bands were observable in Coomassie blue-stained SDS-PAGE gel of glycine extracts (Fig. 1), particularly the proteins of apparent MW 82, 68, and 56 kDa. Western blot and ELISA analyses revealed that the 68-kDa protein band, present in all samples is albumin (Fig. 2 & 3), while the 56-kDa band is most likely heavy-chain Ab fragments that were not removed using Protein L affinity. HC1, HC3, and FN were also found to be adsorbed at minute quantities on the surface of recovered implants (Fig. 2 & 3). Hybridization to serum from a normal female with no silicone breast implant gave negative reaction against any of the tested macromolecules. However, 67%, 33%, and 17% of the patients' sera reacted to native HC1, HC3, and FN, respectively. This demonstrated that Ab to collagen and fibronectin extracellular matrix molecules (ECM) were present at significantly elevated levels in subjects with silicone breast implants. Anti-HSA Abs were not detected in the sera, even though albumin comprises the majority of the implant surface-adherent proteins. Immunoblot also showed additional proteins of interest with MW of approximately 112 and > 205 kDa. The latter was found to be present in all patients with autoimmune or connective tissue diseases. Interestingly, sera from children with VP shunts bound positively for the ~ 82-kDa protein found in some glycine extracts.

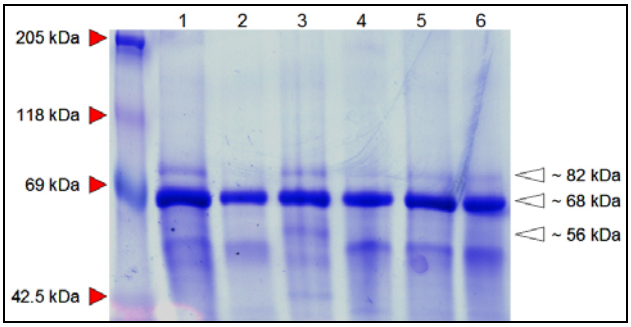

Figure 1. Glycine protein extracts from silicone breast implants

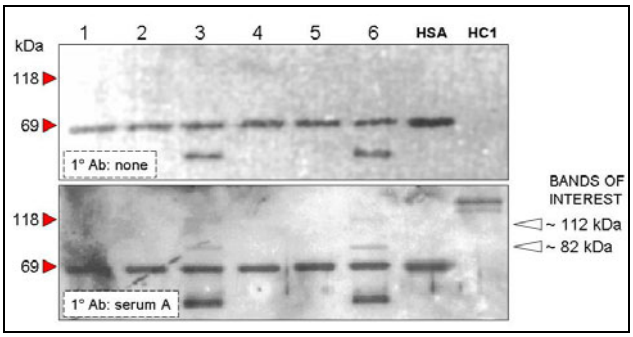

Figure 2. Western blot of extracts hybridized with a patient serum

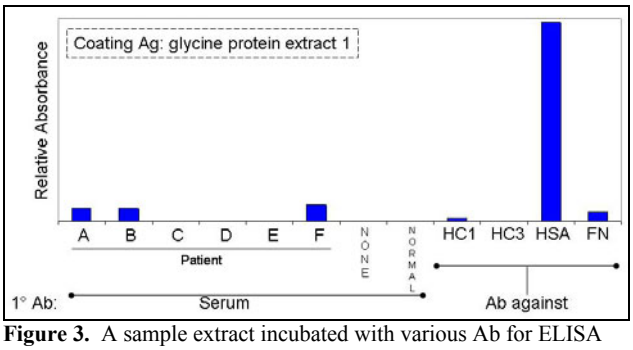

Figure 3. A sample extract incubated with various Ab for ELISA

Conclusions: Silicone polymer may act as surface to which self proteins adhere. Adsorbed proteins may be modified or trigger a yet unknown mechanism causing the generation of autoantibodies which may be relevant in the adverse reactions and implant failure. Characterization of the candidate 82, 112, and > 205 kDa proteins will be the next step.

Reference:

1) VandeVord PJ, Gupta N, Wilson RB, Vinuya RZ, Schaefer CJ, Canady AI, and Wooley PH. 2004. Immune reactions associated with silicone-based ventriculo-peritoneal shunt malfunctions in children. *Biomaterials*. 25:3853.