Review Article

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Breast Implant-Associated Anaplastic Large Cell Lymphoma: What are Researchers Overlooking?

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The relationship between silicone gel-filled breast implants and an increased risk of developing a specific type of anaplastic large cell lymphoma (ALCL) localized to the device site itself is well established [1-4]. What remains unclear are the mechanisms of disease causation that produce this disorder. Research efforts to date have essentially been directed towards identifying anomalies present in a subset of immunocompetent T cells sequestered in the local breast implant milieux. It is generally thought that the combined chronic antigenic stimulation of textured silicone devices and their bacterial biofilms enhance the recruitment, proliferation, clonal expansion and lifespan prolongation of such T cells, all of which eventually leads to malignant transformation. These T cells are accompanied by a variety of other overlapping inflammatory cell infiltrates surrounding the implant that comprise the body's natural response to antigenic stimulation. However, over the first 8-10 years of device implantation, there is a paradoxical and progressive pathological decrease in the concentration of cellular infiltrates surrounding the implant, despite the increasing time-related occurrence of both (a) breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), and (b) progressive worsening of silicone-induced systemic ailments (breast implant illness, or BII). A question to be asked, therefore, about BIA-ALCL is: can such a process possibly be co-orchestrated by silicone induced biochemical disturbances rather than solely by chronic antigenic stimulation? Stated another way, in BIA-ALCL is immunologic exhaustion the only disease producing mechanism?

If research on ALCL is to be redirected, investigators first need to become familiar with two important items: (1) an understanding of the essentiality of the element silicon in health and disease, particularly with regard to silicon's role in the formation of matrix macromolecules; and (2) the toxicity of artificial silicon carbon bonds (the backbone of silicones), none of which are naturally occurring in any living organisms on earth, and all of which are a biochemical mission impossible for life on earth as we know it. One can become familiar with these two topics by perusing four publications referenced at the end of this manuscript [5-8].

The insertion of a silicone gel-filled breast implant into the human body elicits the formation of a fibrocollagenous capsule surrounding the device. Over time changes occur in the capsule that are similar to the process of abscess breakdown in a ruptured appendix. Stated more simply, inevitable capsular failure in one or more locations will prompt the formation of another layer of contractile collagen in the breached zones. As many as eight to ten layers of capsular tissue can form around a breast implant. These "compartments" are devoid of any lymphatic drainage, are hypoxic, and encompass many components including (but not limited to): (a) silicone degradation molecules derived from gel bleed through an intact elastomer envelope (e.g., silanols, which are capable of altering epigenetic factors and, thereby, gene expression, via enhanced DNA methylation); (b) silica (silicon dioxide), leeched from the elastomer envelope, which has a long and sordid history of human misery; (c) living and dead immunocompetent and inflammatory cells; (d) altered matrix macromolecules (aided and abetted by the phenomenon of mechanotransduction); (e) detached particulate matter, surface debris, and chemicals that comprise the ingredients of the textured elastomer envelope; and (f) multiple plasma constituents. Together these are ideal ingredients and conditions for cellular anaplastic transformation.

Consideration must also be given to the relationship between mitochondrial dysfunction and cancer induction [9,10]. Quantum tunneling mediates the process of oxidative phosphorylation, whereby the electron transport system of mitochondria facilitates the production of energy in the form of ATP. The proteins directing the flow of electrons incorporate the cofactors iron and copper in their structure. This is why phosphorus is metal ion bound in energy systems. Although the element silicon forms four bonds like carbon, silicon behaves like a metal at times, and can therefore interfere with enzyme functions involved in electron transport. The net results can be energy disruption and the formation of oxygen derived free radicals. Energy disruption may impair the phosphorylation of the JAK-STAT3 signaling pathway proteins which are (a) intimately involved in gene transcription, and (b) have been shown to be functionally abnormal in the T cell subset that comprises BIA-ALCL. The oxygen derived free radicals may not only damage cells, but they can also facilitate changes in epigenetic factors which, in turn, can adversely alter gene expression in both mitochondrial DNA and cellular DNA. The implications for BIA-ALCL arising from a transformed subset of immunocompetent T cells cohabitating in capsular tissues surrounding an implant are obvious.

A logical question to be asked is: if the element silicon is essential to the formation of matrix macromolecules which, in turn, mediate a myriad of normal physiologic functions in the body, why doesn't silicon simultaneously wreak havoc with the body's biochemistry? There is a vast biochemical difference in living organisms between silicon linked to oxygen versus silicon linked to carbon, the latter of which never spontaneously occurs in nature on our planet earth. Artificial silicon carbon bonds are the backbone of silicones (organosiloxanes), and their degradation products (particularly silanols) are capable of producing dramatic changes in the electromagnetic fields of all life sustaining molecules. Disruptions of overlapping interactions between neurotransmitters, enzymes, proteins, endocrine receptors, DNA, RNA, cytokines, signal transducers, ion channel regulators, clotting factors, mast cells, mucosal barriers, matrix macromolecules, and immunocompetent cells can be legion. Thus, prior assertions by physical chemists that silicones are chemically and biologically inert are no longer tenable.

The complexity of nature far transcends man's ingenuity. Researchers investigating the mechanisms of disease causation in BIA-ALCL might consider biochemical disruptions alongside chronic antigenic stimulation as the driving forces for malignant transformation in this disorder.

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