

Prolactin and silicone breast implants: It takes two to tango

Borba VV^{1,2,3} and Shoenfeld Y^{3,4,5*}

¹Department 'A' of Internal Medicine, Coimbra University Hospital Centre, Coimbra, Portugal

²Faculty of Medicine, University of Coimbra, Coimbra, Portugal

³Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Israel

⁴Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel

⁵Head of "The Mosaic of Autoimmunity" Project in Saint Petersburg University, Russia

Autoimmune diseases affect approximately 5-20% of the developed world population and represent a significant cause of morbidity and mortality among young adults. The etiopathogenesis of autoimmune diseases comprises a combination of genetic, immune, hormonal, and environmental factors, so-called mosaic of autoimmunity. Recently, *Shoenfeld et al.* recognized that different conditions linked to exposure to adjuvants resulted in similar complexes of signs and symptoms and proposed to label this condition "ASIA" (autoimmune/inflammatory syndrome induced by adjuvants) [1], which illustrates the role of environmental immune stimulating agents, or adjuvants, in the instigation of complex autoimmune reactions among individuals bearing a genetic preponderance for autoimmunity [2]. Nowadays, more than 300 patients are listed in the ASIA international registry [3,4]. Although the link between silicon exposure and the development of autoimmune phenomena has been postulated long time ago, there is a growing evidence in the recent literature, supporting this association essentially based on case reports of patients carrying silicone prosthesis [5]. Breast implants contain a type of medical silicone called polydimethylsiloxane (PDMS), which has been widely used in the manufacture of assorted medical devices and, have long been considered biologically inert and harmless. Since the introduction of silicone breast implants in the early 1960s, more than 10 million patients worldwide underwent this procedure, especially in the field of reconstructive surgery. Several cohort studies declare the development of non-specific symptoms like myalgia, chronic fatigue, arthralgia, among others and/or the flowering of autoimmune diseases such as systemic sclerosis, systemic lupus erythematosus, rheumatoid arthritis, and Sjögren's syndrome after the implantation on silicone breast prosthesis [5-8]. A combination of a genetic predisposition (HLA-DR4, DRB1, DR53, DQA1*0102, HLA-C), relevant environmental triggers, history of allergic conditions, established autoimmune diseases or prior documented autoimmune reaction to an adjuvant (implants, vaccines) were considered risk factors for the occurrence of a hyperactive immune response. Obviously, the assumption that an autoimmune disorder would prosper with no relation with the silicon is plausible. Nevertheless, studies found that after replacing silicone-filled by saline-cellulose-mixed implants, approximately 75% of the patients experienced a strong improvement of their complaints [7]. In light of the adjuvant effect of silicones, a few pathways may justify this connection. Silicone leakage, also defined as 'silicone bleeding', represents the migration of relatively low molecular weight silicone compounds through the implant elastomer envelope and may cause a histiocytic reaction with foreign body giant cells forming granulomas. It could increase the exposure of self-antigens

by providing a hydrophobic surface to change the conformation of those proteins thus causing recognition by the immune system and subsequent autoimmune reaction. In addition, it may induce an immunogenic response via cross-reactivity with glucosaminoglycans, a silicon-containing molecule found in connective tissue [9]. On the other hand, several case reports describe postoperative galactorrhoea after aesthetic breast augmentation. The skin incision, the breast manipulation and particularly, the compression of the mammary gland by the implant results in stimulating signal to the hypophysis, and therefore increasing prolactin secretion [10,11]. Years after the procedure, persistent hyperprolactinemia has been documented among those patients, without any other identified cause besides the breast implantation surgery [12]. Prolactin has a recognized immunostimulatory effect, promoting autoimmune phenomena. The prolactin receptor, which is a member of the type 1 cytokine/hematopoietic receptor super-family and is widely expressed through the immune system. Binding of prolactin to its receptor activates downstream signaling pathways that will manipulate immune cells proliferation, differentiation, secretion and survival. In addition, elevated serum levels of prolactin impair B cell clonal deletion, deregulate receptor editing and decrease the threshold for activation of anergic B cells, promoting aberrant reactivity [13]. High prolactin levels have been related in several autoimmune diseases, frequently influencing disease development and perpetuation [14]. In conclusion, silicone breast implants could represent a strong arouse for the development of autoimmune disorders, not only by the surgical procedure *per se*, and the mechanical compression of the implant, stimulating prolactin secretion, but also silicone molecules acting as an adjuvant to abnormal immune reactions. Accordingly, it stands to reason that women with recognized predisposition for autoimmune diseases should be advised by the physicians to avoid silicone breast implantation [7,15].

Conflicts of interest

The authors have no potential conflicts of interest in authorship or publication.

*Correspondence to: Yehuda Shoenfeld, Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center (Affiliated to Tel-Aviv University), Tel: 265601, Israel, E-mail: shoenfel@post.tau.ac.il

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