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Case Report

Rapidly Progressive Systemic Sclerosis after Breast Augmentation Procedure - Autoimmune Syndrome Induced by Adjuvants

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INTRODUCTION

The Autoimmune Syndrome induced by adjuvants (ASIA syndrome) is a recently defined entity. In 2011 Shoenfeld and Agmon-Levin described the occurrence of autoimmune events that were the result of an immune response to adjuvants [1]. Such conditions appeared with a variable latency time and occurred as a result of the interaction between genetic and environmental factors. ASIA is associated with different conditions such as siliconosis, Gulf war syndrome (GWS), macrophagic myofascitis syndrome (MMF) and post-vaccination phenomena [1,2]. One of the main adjuvants currently used in clinical practice is silicon, especially for the placement of implants [2].

Systemic sclerosis (SSc), also known as scleroderma, is a chronic autoimmune disease characterized by vascular dysfunction and progressive fibrosis of the skin and internal organs. The first case reports of SSc after augmentation mammoplasty emerged in 1979 [3,4]. In this paper we report a case of systemic sclerosis developed in a previously healthy young woman after breast augmentation procedure. Written informed consent was obtained from the patient for publication of this case report.

CASE REPORT

Presenting Concerns

35-year-old woman with a record of allergy to naproxen, former smoker with an index pack/years of 10, migraines from the age of 13 and augmentation mammoplasty with silicone prostheses in November 2015. Pregnancy in March 2016 with stillbirth at 41 weeks.

She presented with Raynaud phenomenon lasting for 3 years (from January 2016), a hypertrophic skin area in the metacarpophalangeal joint of the 3rd finger of the right hand and xerosis with roughness, especially in the right arm.

The patient was initially evaluated by Dermatology with skin findings suggesting limited systemic sclerosis. Based on these findings, she started treatment with hydroxychloroquine, nifedipine and acetylsalicylic acid. She developed distal sharpening of fingers, nose sharpening and skin thickening on both forearms and was referred to Rheumatology department.

Clinical and lab findings

Physical examination revealed sclerodactyly and skin induration in both hands extended to the forearms, microstomia and facial telangiectasia.

Laboratory tests detected positive antinuclear antibodies at a titer of 1:640, with a speckled pattern. The specific test panels for systemic sclerosis-associated antibodies showed anti-RNA Polymerase III at a titer of 1:640. No additional abnormalities were found.

Nailfold capillaroscopy showed early pattern of scleroderma. High-resolution computed tomography (HRCT) was normal. Lung function testing showed no ventilation disorders, vital capacity was 90%. Echocardiography demonstrated no evidence of pulmonary hypertension or any other abnormalities.

Due to patient`s background of Raynaud phenomenon initiating after prosthetic breast implant, HLA study was performed with a genotype HLA DRB1, HLA DQB1 compatible with ASIA diagnosis.

Based upon the clinical and complementary tests findings we diagnosed systemic scleroderma induced by breast implants in

the course of ASIA syndrome and recommended removal of the breast implants due to rapid clinical progression of the disease. The patient started on methotrexate, folinic acid supplementation and nifedipine.

Follow up and outcomes

One year after removal of both breast implants, the patient referred clear improvement in skin hardening, microstomia, Raynaud phenomenon and fatigue. Currently the patient remains stable with the treatment mentioned above.

DISCUSSION

To date, there are no blood markers or "screening" test for ASIA diagnosis. Clinicians need to be aware of possible adjuvant exposures in the patient antecedents because symptoms may appear many years after exposure to an adjuvant substance.

Our patient fulfilled the diagnostic criteria for ASIA syndrome [1]. Including: 1) Exposure to an external stimulus (infection, vaccine, silicone, adjuvant) prior to clinical manifestations 2) The appearance of 'typical' clinical manifestations. 3) Removal of inciting agent inducing improvement. 4) Specific HLA (i.e., HLA DRB1, HLA DQB1) presence. 5) Evolvement of an autoimmune disease (i.e., multiple sclerosis, systemic sclerosis).

Currently, pathophysiology of ASIA syndrome continues to be investigated, it is now known that adjuvants may act as a molecular pattern associated with pathogen, with the consequent activation of pattern recognition receptors and release of pro-inflammatory cytokines such as TNF-alpha, IL-1, IL-6, IFN-gamma. These cytokines induce maturation of monocytes and dendritic cells, with enhanced expression of co-stimulatory molecules and of the major histocompatibility complex, which together with IL-6, promotes the secretion of pathologic auto-antibodies [5]. This mechanism is observed in patients with genetic predisposition as indicated by the strong association with HLA-DRB1 with ASIA syndrome. Noteworthy, the same HLA has been found in patients who developed an autoimmune disease following vaccine administration [6].

Different meta-analyses have been published, describing the association between SSc and breast implants. In 2017 Rubio-Rivas et al., showed increased risk of SSc in patients with silicone breast implant (SBI), when case-control studies were taken into consideration (relative risk [RR]: 1.68, 95% confidence interval [CI]: 1.65–1.71), but no increased risk in cohort studies (RR: 2.13, 95% CI: 0.86–5.27) [7]. A systematic literature review showed that up to 75% of complaints related to silicon breast implants disappeared after implant removal [8]. However, other study by Colaris et al. [4], showed that in 26% of patients the improvement after implant removal was only temporary.

CONCLUSIONS

We present a patient with SSc presenting the risk-related HLA associated with the ASIA syndrome. In patients with autoimmune events, it is advised to obtain a complete medical history, considering possible exposure to adjuvants, to guide diagnosis of ASIA syndrome and to indicate removal of the adjuvant or avoidance whenever possible.

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