

Autoimmune/inflammatory syndrome induced by adjuvants (Shoenfeld's syndrome): clinical and immunological spectrum

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An adjuvant is a substance that enhances the antigen-specific immune response, induces the release of inflammatory cytokines, and interacts with Toll-like receptors and the NALP3 inflammasome. The immunological consequence of these actions is to stimulate the innate and adaptive immune response. The activation of the immune system by adjuvants, a desirable effect, could trigger manifestations of autoimmunity or autoimmune disease. Recently, a new syndrome was introduced, autoimmune/inflammatory syndrome induced by adjuvants (ASIA), that includes postvaccination phenomena, macrophagic myofasciitis, Gulf War syndrome and siliconosis. This syndrome is characterized by nonspecific and specific manifestations of autoimmune disease. The main substances associated with ASIA are squalene (Gulf War syndrome), aluminum hydroxide (postvaccination phenomena, macrophagic myofasciitis) and silicone with siliconosis. Mineral oil, guaiacol and iodine gadital are also associated with ASIA. The following review describes the wide clinical spectrum and pathogenesis of ASIA including defined autoimmune diseases and nonspecific autoimmune manifestations, as well as the outlook of future research in this field.

KEYWORDS: ASIA • environmental factors • Gulf War syndrome • human adjuvant disease • macrophagic myofasciitis syndrome • mineral oil • postvaccination phenomena • silicone

Autoimmune diseases (AID) are the result of interactions between genetic and environmental factors with innate and adaptive immune activation response. In relation to environment, an important problem is to identify the criteria of patients in whom it plays a causative role [1].

Recent findings from a National Institute of Environmental Health Sciences Expert Panel Workshop concluded that crystalline silica, solvents, smoking and UV radiation exposure can contribute to the development of several AID [2]. In experimental models, chemical, physical and biological agents induce and/or exacerbate autoimmunity. Examples include mercury, pristane, silica, gold, UV radiation and infection with *Streptococcus* or Coxsackie B virus and so on [3].

Recently, a new syndrome was introduced termed autoimmune/inflammatory syndrome induced by adjuvants (ASIA). The environmental factors that participate in ASIA are squalene

associated with Gulf War syndrome (GWS), aluminum hydroxide (Alum) with postvaccination phenomena and macrophagic myofasciitis syndrome (MMF) and silicone with siliconosis [4]. In addition, environmental factors that include mineral oil, guaiacol (metoxiphenol) and iodine gadital (this substance is a mix of guaifenesine, proxyphylline, malcate of clorphenamine [mucolytic, bronchodilator, antihistaminic, respectively]) plus mineral oil are associated with new models of ASIA [5]. The aim of this review is to analyze the role of environmental factors in the pathogenesis and the clinical spectrum of ASIA. In this review, the main clinical syndromes discussed are:

- Postvaccination phenomena associated with rheumatic diseases that include vasculitis, systemic lupus erythematosus (SLE), inflammatory myopathy (IM), and rheumatoid