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[Lessons from macrophagic myofasciitis: towards definition of a vaccine adjuvant-related syndrome].

[Article in French]

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Source

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Abstract

Macrophagic myofasciitis is a condition first reported in 1998, which cause remained obscure until 2001. Over 200 definite cases have been identified in France, and isolated cases have been recorded in other countries. The condition manifests by diffuse myalgias and chronic fatigue, forming a syndrome that meets both Center for Disease Control and Oxford criteria for the so-called chronic fatigue syndrome in about half of patients. One third of patients develop an autoimmune disease, such as multiple sclerosis. Even in the absence of overt autoimmune disease they commonly show subtle signs of chronic immune stimulation, and most of them are of the HLADRB1*01 group, a phenotype at risk to develop polymyalgia rheumatica and rheumatoid arthritis. Macrophagic myofasciitis is characterized by a stereotyped and immunologically active lesion at deltoid muscle biopsy. Electron microscopy, microanalytical studies, experimental procedures, and an epidemiological study recently demonstrated that the lesion is due to persistence for years at site of injection of an aluminum adjuvant used in vaccines against hepatitis B virus, hepatitis A virus, and tetanus toxoid. Aluminum hydroxide is known to potently stimulate the immune system and to shift immune responses towards a Th-2 profile. It is plausible that persistent systemic immune activation that fails to switch off represents the pathophysiologic basis of chronic fatigue syndrome associated with macrophagic myofasciitis, similarly to what happens in patients with post-infectious chronic fatigue and possibly idiopathic chronic fatigue syndrome. Therefore, the WHO recommended an epidemiological survey, currently conducted by the French agency AFSSAPS, aimed at substantiating the possible link between the focal macrophagic myofasciitis lesion (or previous immunization with aluminium-containing vaccines) and systemic symptoms. Interestingly, special emphasis has been put on Th-2 biased immune responses as a possible explanation of chronic fatigue and associated manifestations known as the Gulf war syndrome. Results concerning macrophagic myofasciitis may well open new avenues for etiologic investigation of this syndrome. Indeed, both type and structure of symptoms are strikingly similar in Gulf war veterans and patients with macrophagic myofasciitis. Multiple vaccinations performed over a short period of time in the Persian gulf area have been recognized as the main risk factor for Gulf War syndrome. Moreover, the war vaccine against anthrax, which is administered in a 6-shot regimen and seems to be crucially involved, is adjuvanted by aluminium hydroxide and, possibly, squalene, another Th-2 adjuvant. If safety concerns about long-term effects of aluminium hydroxide are confirmed it will become mandatory to propose novel and alternative vaccine adjuvants to rescue vaccine-based strategies and the enormous benefit for public health they provide worldwide.

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