

Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminium hydroxide in muscle

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Summary

Macrophagic myofasciitis (MMF) is an emerging condition of unknown cause, detected in patients with diffuse arthromyalgias and fatigue, and characterized by muscle infiltration by granular periodic acid-Schiff's reagent-positive macrophages and lymphocytes. Intracytoplasmic inclusions have been observed in macrophages of some patients. To assess their significance, electron microscopy was performed in 40 consecutive cases and chemical analysis was done by microanalysis and atomic absorption spectrometry. Inclusions were constantly detected and corresponded to aluminium hydroxide, an immunostimulatory compound frequently used as a vaccine adjuvant. A lymphocytic component was constantly observed in MMF lesions. Serological tests were compatible with exposure to aluminium hydroxide-

containing vaccines. History analysis revealed that 50 out of 50 patients had received vaccines against hepatitis B virus (86%), hepatitis A virus (19%) or tetanus toxoid (58%), 3–96 months (median 36 months) before biopsy. Diffuse myalgias were more frequent in patients with than without an MMF lesion at deltoid muscle biopsy ($P < 0.0001$). Myalgia onset was subsequent to the vaccination (median 11 months) in 94% of patients. MMF lesion was experimentally reproduced in rats. We conclude that the MMF lesion is secondary to intramuscular injection of aluminium hydroxide-containing vaccines, shows both long-term persistence of aluminium hydroxide and an ongoing local immune reaction, and is detected in patients with systemic symptoms which appeared subsequently to vaccination.

Keywords: inflammatory myopathy; drug adverse effect; macrophage; vaccine; aluminium hydroxide

Abbreviations: HAV = hepatitis A virus; HBV = hepatitis B virus; MMF = macrophagic myofasciitis; PAS = periodic acid-Schiff reagent; TT = tetanus toxoid

Introduction

Macrophagic myofasciitis (MMF) is a recently recognized entity, emerging in 1993 from France (Gherardi *et al.*, 1998). Affected patients have diffuse steroid-responsive arthromyalgias and marked fatigue as their main clinical symptoms.

Deltoid muscle biopsy shows stereotypical perimuscular infiltration by large macrophages with a finely granular periodic acid-Schiff's reagent (PAS)-positive content intermingled with lymphocytic infiltrates, and inconspicuous