



Long-term persistence of vaccine-derived aluminum hydroxide is associated with chronic cognitive dysfunction

Maryline Couette^{a,c}, Marie-Françoise Boisse^{a,c}, Patrick Maison^{a,d,2}, Pierre Brugieres^e, Pierre Cesaro^{a,c}, Xavier Chevalier^f, Romain K. Gherardi^{b,g,h}, Anne-Catherine Bachoud-Levi^{a,c,1}, François-Jérôme Authier^{b,g,h,1,*}

^aINSERM, Unite U955, Team 1, Creteil F-94010, France

^bINSERM, Unite U955, Team 10, Creteil F-94010, France

^cUniversité Paris 12, Faculté de Médecine, AP-HP, Groupe Henri-Mondor Albert-Chenevier, Department of Neurology, Creteil F-94010, France

^dUniversité Paris 12, Faculté de Médecine, AP-HP, Groupe Henri-Mondor Albert-Chenevier, Department of Biostatistics, Creteil F-94010, France

^eUniversité Paris 12, Faculté de Médecine, AP-HP, Groupe Henri-Mondor Albert-Chenevier, Department of Neuroradiology, Creteil F-94010, France

^fUniversité Paris 12, Faculté de Médecine, AP-HP, Groupe Henri-Mondor Albert-Chenevier, Department of Rheumatology, Creteil F-94010, France

^gUniversité Paris 12, Faculté de Médecine, AP-HP, Groupe Henri-Mondor Albert-Chenevier, Department of Histology, Creteil F-94010, France

^hReference Center for Neuromuscular Diseases Garches-Necker-Mondor-Hendaye, Creteil F-94010, France

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ABSTRACT

Macrophagic myofasciitis (MMF) is an emerging condition, characterized by specific muscle lesions assessing long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization. Affected patients mainly complain of arthromyalgias, chronic fatigue, and cognitive difficulties. We designed a comprehensive battery of neuropsychological tests to prospectively delineate MMF-associated cognitive dysfunction (MACD). Compared to control patients with arthritis and chronic pain, MMF patients had pronounced and specific cognitive impairment. MACD mainly affected (i) both visual and verbal memory; (ii) executive functions, including attention, working memory, and planning; and (iii) left ear extinction at dichotic listening test. Cognitive deficits did not correlate with pain, fatigue, depression, or disease duration. Pathophysiological mechanisms underlying MACD remain to be determined. In conclusion, long-term persistence of vaccine-derived aluminum hydroxide within the body assessed by MMF is associated with cognitive dysfunction, not solely due to chronic pain, fatigue and depression.

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1. Introduction

Macrophagic myofasciitis (MMF) is a rare condition characterized by highly specific myopathological alterations at deltoid muscle biopsy, recognized in 1998 (Rare disease #ORPHA592, www.orpha.net) [1], and subsequently shown to assess long-term persistence of vaccine-derived aluminum hydroxide nanoparticles within macrophages at the site of previous intramuscular injections [2]. Clinical manifestations observed in adult patients typically include chronic arthromyalgias and fatigue [3,4], appearing in a delayed fashion after the last aluminum-containing vaccine injection [2]. According to records of the French patient association E3M, 78% of affiliated patients withdrew their professional activity

after the onset of clinical manifestations [5], due to these disabling symptoms combined with intellectual disturbance affecting both memory and ability to concentrate. In particular, patients frequently report on difficulties in sustaining their attention on tasks of daily living, such as following a conversation or efficiently allocating their attention resources to different simultaneous stimuli.

Until now, cognitive impairment in MMF patients was downplayed and left out of medical attention, and, indeed, an obvious link between focal intramuscular accumulation of aluminum-loaded macrophages and cerebral dysfunction is missing, despite growing evidence that nanoparticles have the unique capacity to spread throughout the body and cross the blood brain barrier [6]. Notably, there are marked inter-individual variations in the ability to clear out aluminum from the body, and the MMF lesion from the injected muscle [7]. Cognitive complaints of MMF patients are similar to those reported by the multiple sclerosis (MS) [8], and marked fatigue may occur in both conditions [4,9]. In addition, MMF patients suffer from musculoskeletal pain (up to 88%) and chronic fatigue (duration >6 months; up to 93%) [4]. Fatigue was

* Corresponding author. Address: INSERM, Unite U955, Team 10, Creteil F-94010, France. Tel.: +33 1 4981 2735; fax: +33 1 4981 2733.

E-mail address: authier@univ-paris12.fr (F.-J. Authier).

¹ A.C.B.L. and F.J.A. have equally contributed to this work.

² Conducted the statistical analysis (Biostatistics, Henri Mondor Hospital, APHP).