

Highly delayed systemic translocation of aluminum-based adjuvant in CD1 mice following intramuscular injections

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Abstract

Concerns regarding vaccine safety have emerged following reports of potential adverse events in both humans and animals. In the present study, alum, alum-containing vaccine and alum adjuvant tagged with fluorescent nanodiamonds were used to evaluate i) the persistence time at the injection site, ii) the translocation of alum from the injection site to lymphoid organs, and iii) the behavior of adult CD1 mice following intramuscular injection of alum (400 µg Al/kg). Results showed for the first time a strikingly delayed systemic translocation of adjuvant particles. Alum-induced granuloma remained for a very long time in the injected muscle despite progressive shrinkage from day 45 to day 270. Concomitantly, a markedly delayed translocation of alum to the draining lymph nodes, major at day 270 endpoint, was observed. Translocation to the spleen was similarly delayed (highest number of particles at day 270). In contrast to C57BL/6J mice, no brain translocation of alum was observed by day 270 in CD1 mice. Consistently neither increase of Al cerebral content, nor behavioral changes were observed. On the basis of previous reports showing alum neurotoxic effects in CD1 mice, an additional experiment was done, and showed early brain translocation at day 45 of alum injected subcutaneously at 200 µg Al/kg. This study confirms the striking biopersistence of alum. It points out an unexpectedly delayed diffusion of the adjuvant in lymph nodes and spleen of CD1 mice, and suggests the importance of mouse strain, route of administration, and doses, for future studies focusing on the potential toxic effects of aluminum-based adjuvants.

Keywords: Alum; CD1 mice; Delayed-translocation; Fluorescent-nanodiamonds; Neurotoxicity; Vaccine-adjuvant.