Behavioral abnormalities in female mice following administration of aluminum adjuvants and the human papillomavirus (HPV) vaccine Gardasil. - PubMed

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Abstract

Vaccine adjuvants and vaccines may induce autoimmune and inflammatory manifestations in susceptible individuals. To date most human vaccine trials utilize aluminum (Al) adjuvants as placebos despite much evidence showing that Al in vaccine-relevant

exposures can be toxic to humans and animals. We sought to evaluate the effects of Al adjuvant and the HPV vaccine Gardasil versus the true placebo on behavioral and inflammatory parameters in female mice. Six-week-old C57BL/6 female mice were injected with either, Gardasil, Gardasil + pertussis toxin (Pt), Al hydroxide, or, vehicle control in amounts equivalent to human exposure. At 7.5 months of age, Gardasil and Al-injected mice spent significantly more time floating in the forced swimming test (FST) in comparison with vehicle-injected mice (Al, $p = 0.009$; Gardasil, $p = 0.025$; Gardasil + Pt, $p = 0.005$). The increase in floating time was already highly significant at 4.5 months of age for the Gardasil and Gardasil + Pt group ($p \leq 0.0001$). No significant differences were observed in the number of stairs climbed in the staircase test which measures locomotor activity. These results indicate that differences observed in the FST were unlikely due to locomotor dysfunction, but rather due to depression. Moreover, anti-HPV antibodies from the sera of Gardasil and Gardasil + Pt-injected mice showed cross-reactivity with the mouse brain protein extract. Immunohistochemistry analysis revealed microglial activation in the CA1 area of the hippocampus of Gardasil-injected mice. It appears that Gardasil via its Al adjuvant and HPV antigens has the ability to trigger neuroinflammation and autoimmune reactions, further leading to behavioral changes.

KEYWORDS:

ASIA syndrome; Aluminum; Autoantibodies; Autoimmunity; Gardasil; Neuroinflammation

Publication type, MeSH terms, Substances

Publication type

- Research Support, Non-U.S. Gov't

MeSH terms

- Adjuvants, Immunologic/adverse effects*
- Adjuvants, Pharmaceutic/adverse effects*
- Aluminum Hydroxide/adverse effects*
- Animals
- Antibodies, Viral/blood
- Antigens, Viral/immunology
- Autoantibodies/blood
- Behavior, Animal/drug effects
- Capsid Proteins/immunology
- Female
- Human Papillomavirus Recombinant Vaccine Quadrivalent, Types 6, 11, 16, 18/adverse effects*
- Locomotion/drug effects
- Mice, Inbred C57BL
- Oncogene Proteins, Viral/immunology
- Recognition (Psychology)/drug effects
- Swimming

Substances

- Adjuvants, Immunologic
- Adjuvants, Pharmaceutic
- Antibodies, Viral
- Antigens, Viral
- Autoantibodies
- Capsid Proteins
- HPV L1 protein, Human papillomavirus
- Human Papillomavirus Recombinant Vaccine Quadrivalent, Types 6, 11, 16, 18
- Oncogene Proteins, Viral
- Aluminum Hydroxide

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