

Are post-vaccinal persistent itching nodules related to the use of local anaesthetic patches? A hypothesis to be confirmed

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Persistent itching nodules or granulomas have been described at the injection sites of immunizations containing aluminium hydroxide as an adjuvant since the 1960s. Over the last 10 years, such skin reactions have unexpectedly increased with the use of adsorbed vaccines (1), and a recent study reported an incidence of persistent itching nodules of 0.8% in children vaccinated with adsorbed vaccines from a single manufacturer in Sweden (2). Clinically, the lesions may present as very itchy subcutaneous nodules, excoriated papulo-nodules or lichenified eczema plaques at the injection site. When performed, histopathology may show the presence of aluminium granulomas (3). Usually, the nodules regress spontaneously within a period of several months to several years.

Case Report

We studied a consecutive case series of 6 children (mean age, 26 months) who presented with itching nodules after immunization with aluminium hydroxide-containing vaccines. In all children, aluminium contact allergy was assessed with either reaction to aluminium Finn Chambers[®] or positive epicutaneous tests with aluminium chloride 2% pet. and aluminium metal (Chemotechnique Diagnostics[®], Malmö, Sweden) (4). As we suspected exposure to a lidocaine/prilocaine patch

(EMLA[®] patch; AstraZeneca, Sodertalje, Sweden) to be a possible cause of this process, owing to its aluminium packaging, we reviewed the case notes of all children with persistent itching nodules, and found that all had received an EMLA[®] patch prior to the immunization. Therefore, we decided to investigate the presence of aluminium in EMLA[®] patches in the Hydrology/Environment reference laboratory at the University in Bordeaux. We found that the disc matrix of EMLA[®] patches could expose the skin to $8.1 \pm 2.6 \mu\text{g}$ (mean $\pm$ standard deviation) of aluminium for a calculated surface of approximately 10 cm^2 (methodology available on request). Thus, the disc matrix in close contact with the skin can release aluminium from the laminate backing.

Discussion

To date, there has been no plausible hypothesis for the increasing incidence of persistent itching nodules. Some authors have hypothesized that subcutaneous injection may be responsible for this effect (3). However, a study has found similar rates of persistent itching nodules in children immunized by the subcutaneous and the intramuscular routes, arguing against this hypothesis (2). It is of note that persistent itching nodules and contact allergy to aluminium have both been reported in patients who have been hyposensitized with allergen extracts containing aluminium (5, 6).

We hypothesize that the aluminium found in the EMLA[®] patch disc matrix is primarily responsible for the induction of sensitization, with elicitation by the aluminium contained in the vaccine. In addition, the timing of vaccination corresponds to a period of skin barrier maturation, which may enhance the access of environmental molecules to the skin immune system (7).

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The increased incidence of persistent itching nodules since 2000 may thus be linked to an increase in the use of EMLA[®] patches prior to vaccination. In this case series, causality cannot be proved, but we strongly believe that this hypothesis merits further attention and discussion within the medical community. Clarifying this

hypothesis with further experimental and epidemiological case–control studies will be helpful for explaining an important public health issue, because vaccination side effects may result in poor family compliance with the vaccination calendar, and the potential reappearance of old, preventable diseases.

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