INTRODUCTION

Adverse reactions to vaccines are highly varied, ranging from mild local reactions to fatal outcomes. Cutaneous adverse reactions after exposure to aluminum-containing vaccines are usually benign, mostly consisting of mild transient reactions occurring at the site of injection. The development of painful and itching persistent aluminum induced subcutaneous nodules, extensive limb swelling, cold panniculitis or macrophagic myofasciitis is a rare event. (1) The observation of aluminum induced cutaneous B-cell lymphoid hyperplasia, showing prominent germinal centre formation in sites other than the vaccination injection sites is an exceedingly rare phenomenon. (2-4) Specific aluminum (Morel) stains, electronic microscopy, microanalysis and immunologic cutaneous provocation tests may permit to demonstrate the responsibility of aluminum hydroxide in such cutaneous reactions.

CASE REPORT

CUTANEOUS LESIONS

An otherwise healthy, 25 year-old Caucasian woman developed an erythematous, infiltrated plaque, five centimetres in diameter on the outer aspect of the right arm developing at the site of injection one year after the tetanus toxoid vaccine administration, (fig. 1). During the following years three additional erythematous, infiltrated nodules progressively appeared on the upper lip (fig.2), preauricular (fig.3) and temporal areas (fig.4). These lesions had showed occasional and recurrent self-limited inflammatory episodes becoming itchy, erythematous and more infiltrated. No precipitating factors for such episodes could be recorded. Several therapeutic approaches with topical, intralesional or oral corticosteroids, radiotherapy or even surgical excision have been reported.

HISTOPATHOLOGICAL AND LABORATORY FINDINGS

Histopathological evaluation revealed a deep dense nodular and diffuse dermal lymphohistiocytic infiltration with prominent germinal centre formation and a peripheral lymphoid infiltrate with occasional eosinophils. No cellular atypia was noted (fig. 5, 6). Immunohistochimical studies, disclosed a mixed component of B-cells (CD79a, CD20), with regular, well-defined lymphoid follicular distribution germinal (CD10, Bcl-2), and a peripheral T-cell component (CD3, CD5, CD43). No immunoglobulin light chain restriction was present. B-cell (FR1, FR2, FR3) and T-cell (TCR gamma and beta-chains) genotypic studies failed to show any evidence of clonal proliferation.

DISCUSSION AND CONCLUSIONS

Cutaneous B-cell lymphoid hyperplasia, also called cutaneous B-cell pseudolymphoma has occasionally been reported to develop several months or years at sites of previous vaccination. In only rare instances these lesions have been observed to develop also at distant sites. These lesions are clinically manifested as painful and/or itching nodules or infiltrated plaques. Aluminium hydroxide, used as adjuvant for vaccines has been suggested to be the responsible factor. Aluminium hydroxide has been shown to induce Th2 response and to up-regulate accessory properties of human monocytes by IL-4 dependent mechanism. (6) In this case, cutaneous hypersensitivity test (the recommended diagnostic test for granulomatous reactions) with the entire tetanus toxoid vaccine and aluminium hydroxide 1:100 reproduced the delayed granulomatous hypersensitivity reaction. Negative patch test is not a rare phenomenon, since contact hypersensitivity to aluminum has been scarcely documented in granulomatous reactions. Sequential histopathologic studies have shown an initial histiocytic foreign body reaction (fig.5), followed by a progressive associated lymphoid infiltration (fig.6), which in late lesions adopts a pseudolymphomatous pattern (fig.5, 6). B-cell lymphoid hyperplasia has usually a benign course, although in a small number of cases, the lesions become persistent and in rare instances the development of a true primary cutaneous B-cell lymphoma. The treatment is often difficult and non-constant results to either topical or intralional corticosteroids, antimalarials, local radiotherapy or even surgical excision have been reported.