

# CUTANEOUS PSEUDOLYMPHOMA SECONDARY TO ALUMINIUM-CONTAINING TETANUS TOXOID VACCINE

Parera E, Sánchez-Schmidt J, Gallardo F, Conde D, Barranco C, Romagosa V\*, Servitje O\*, Giménez-Arnau A, Pujol RM.

Departments of Dermatology, Pathology and Pharmacy. Hospital del Mar. IMAS.  
Department of Dermatology and Pathology, Hospital de Bellvitge.\* Barcelona. Spain.

## INTRODUCTION

Adverse reactions to vaccines are highly varied, ranging from mild local reactions to fatal outcomes. Cutaneous adverse events after exposure to aluminium-containing vaccines are usually benign, mostly consisting of mild transient reactions occurring at the site of injection. The development of painful and itching persistent aluminium induced subcutaneous nodules, extensive limb swelling, cold panniculitis or macrophagic myofasciitis are rare

events (1). The observation of aluminium 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 aluminium (Morin) stains, electronic microscopy, microanalysis and immunologic cutaneous provocation tests may permit to demonstrate the responsibility of aluminium 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, and antimalarials, have only achieved a temporary relief, but failed to avoid the development of new inflammatory episodes. After seven years of follow-up the lesions remained unmodified showing occasional inflammatory changes.

### HISTOPATHOLOGICAL AND LABORATORY FINDINGS

Histopathological evaluation revealed a deep dense nodular and diffuse dermal lymphohistiocytic infiltration with prominent germinal center formation and a peripheral lymphoid infiltrate with occasional eosinophils. No cellular atypia was noted (fig. 5,6). Immunohistochemical studies, disclosed a mixed component of B-cells (CD79a, CD20), with regular, well-defined lymphoid follicular distribution germinal (CD10, Bcl-6), 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 a monoclonal population. Serologic studies for of *Borrelia burgdorferi* were negative. A complete haematological and biochemical survey disclosed no abnormalities. Radiological studies including chest X-ray films and abdominal CAT scan were normal.



Fig.5. Lip lesion; dermal infiltrate shows a lymphoid follicular architecture, HEx2.

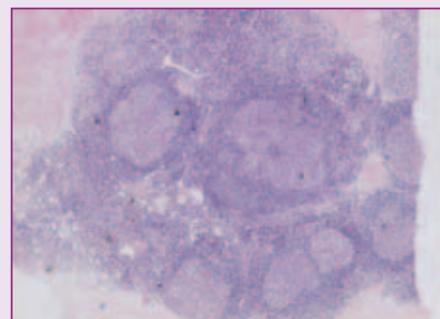


Fig.6. Lip lesion; germinal centers and a prominent perifollicular infiltrate, HEx10.



Fig.2. Facial erythematous infiltrated nodule.



Fig.3. Preauricular plaque.



Fig.4. Temporal infiltrated alopecic plaque.

### IMMUNOLOGIC STUDY (table 1)

Immunologic Study	
1. Patch test	negative
2. Prick test	negative
3. Intradermal test	positive

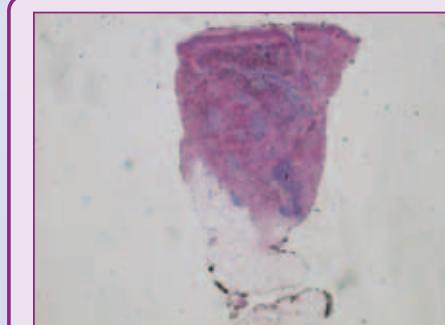


Fig.7. A delayed nodule formation 21 days after the tetanus toxoid intradermal test showed a lymphoid infiltration and granulomatous reaction with central necrosis.



Fig.8. A delayed papule formation was initiated at 48 hours and distant erythematous papules also at the contralateral forearm from the aluminium hydroxide intradermal test.

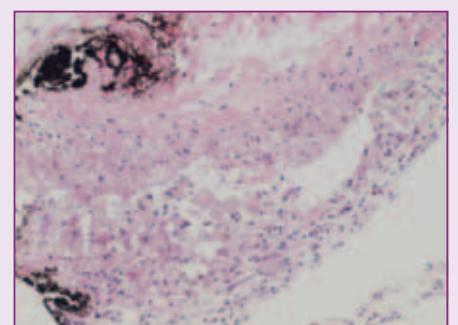


Fig.9. Eight days after the aluminium hydroxide intradermal biopsy showed eosinophilic material that initiate a foreign body reaction with eosinophils.

## DISCUSSION AND CONCLUSIONS

Cutaneous B-cell lymphoid hyperplasia, also called cutaneous B-cell pseudolymphoma has occasionally been reported to develop after 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, intradermal 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 aluminium has been scarcely documented in granulomatous reactions. Sequential histopathologic studies have shown an initial histiocytic foreign body reaction (fig.9), followed by a progressive associated lymphoid infiltration (fig.7), 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 can occur. The treatment is often difficult and non-constant results to either topical or intralesional corticosteroids, antimalarials, local radiotherapy or even surgical excision have been reported.

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