The appearance of atopic dermatitis after primary BCG vaccination in a male infant

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SUMMARY

The case of a 22 month old male infant is reported, who underwent BCG vaccination five days after his birth. Almost 4 months after the vaccination, an abscess developed at the site of the injection. Mildly itching, circular to oval macular lesions appeared first surrounding the abscess, then spread over the entire body. The rash was successfully treated with topical emollients and mometasone furoate ointment. The infant displayed white dermographism, and his mother had a history of atopic dermatitis. The possible role of underlying immunological factors are discussed in relation to the symptomatology.

KEY WORDS

BCG vaccination, primary, male infant, atopic dermatitis

Introduction

Lymphadenitis and abscess formation in the region of the vaccination or in the axilla occur rather frequently as complications following BCG vaccination.. Rarely a tuberculotic infection such as lupus vulgaris or BCG osteitis or sepsis occur (1,2,3,4). Recently, two children with atopic dermatitis (AD) have been reported in whom eczematous exacerbation developed after BCG revaccination (5).

The present paper reports the case of a male infant suffering from the characteristic rashes of AD, which developed primarily around an abscess at the primary BCG vaccination site.

Case report

Following an unremarkable pregnancy and perinatal period, the currently 22 month-old infant boy underwent a BCG vaccination on his left upper arm at five days after his birth. Approximately four months later, he was admitted to our department (FH) upon developing a sensitive protrusion with a diameter of 10 mm and eczematous skin symptoms in the vaccination area, as well as slightly erythematous, dry skin patches on the face, trunk, and extremities. The infant's mother reported that a fluid-oozing nodule had developed on the skin covering the left deltoid muscle at the site of the injection. Subsequently, nearly 4 months after the

vaccination, an itchy focus of 40 x 50 mm in diameter, with a red margin and crust-covered center developed. Thereafter, she noticed additional erythematous patches on the baby's body.

As a child, the infant's mother was treated for AD, whereas its father and both siblings are healthy.

Dermatological status

An abscess of 10 mm diameter was observed on the left upper arm directly over the m. deltoideus. The surrounding skin (40 x 25 mm) was slightly elevated and covered with a yellowish crust. The lesion was sharply demarcated and pruritic. Vitropression was negative. Additionally, small red and mildly pruritic, slightly desquamated and infiltrated patches and plaques 5 to 30 mm in diameter were observed. The irregular, sharp margins were observed on the face, in the area above the chin and periorally, as well as on the back and scattered over the right upper and both lower limbs (Figures 1 and 2.). A white dermographism was expressed.

Laboratory tests

ESR: 5 mm/l hour; Hb: 114 g/l; Hct: 34.6%; leukocytes: 17.000; thrombocytes: 322.000. Differential blood count: segmented neutrophils 58%, lymphocytes: 30%, monocytes: 4%, eosinophils: 8%. Serum antibodies: IgG: 7.8 g/l; IgA: 0.68 g/l; IgM: 0.49 g/l; total IgE: 100 IU/ml (normal ranges). SGOT: 32 U/l; SGPT: 26 U/l; serum Fe: 7.9 µmol/l; serum Cu: 12.9 µmol/l (normal ranges). Urine bacteriology: sterile; throat flora: normal values; bacteriological cultures from involved skin areas: E.coli.

The abscess at the vaccination site was surgically incised and excochleated. The subsequently administered repeated dressings with polyvidon-iodine ointment resulted in a fast drying and epithelization. The skin signs distributed widely over the body were interpreted as AD, therefore emollients in addition to momethason furoate (once daily) were initiated. A gradual improvement followed, and two weeks later the patient was entirely asymptomatic. No symptoms or complaints were present at the follow-up examinations at two weeks, two months, and one year. In the BCG vaccination area, a pea-sized scar (fibrous nodule) was palpable.

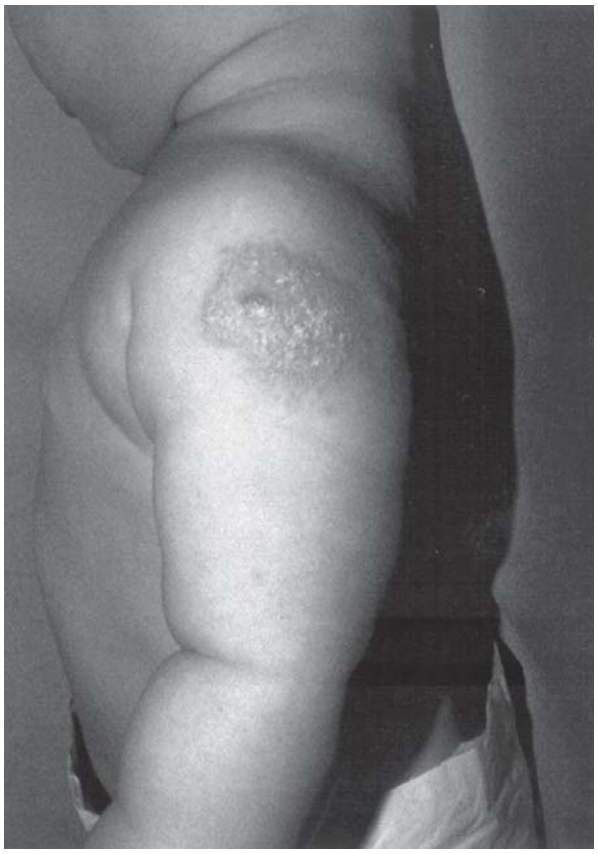

Figure 1. Around the scar on the left upper arm, a 40 x *25* mm plaque with a yellowish crust-covered surface is visible

Discussion

BCG vaccination can lead to several complications, of which lupus vulgaris (1,2,3,4,5,6), disseminated BCG infection in conjunction with hyper-IgE syndrome (7), and osteomyelitis (8) are mentioned in the literature. Upon reporting complications related to BCG vaccination, some authors question its harmlessness (9). Others, describing lupus vulgaris following intracutaneous BCG immunization, maintain that BCG is one of the safest and most effective vaccinations available (10).

In the case of the infant presented, an abscess developed at the primary BCG vaccination site, and AD symptoms (beginning around the abscess) were observed later. The question arises whether this was a casual association or indeed a causal connection between BCG vaccination and development of AD in an infant with a positive family history (mother). Data concerning this question are scant and contradictory. A recent study reported the recurrence of AD following BCG revaccination (5). Japanese authors claim that early BCG vaccination can prevent atopic diseases (11), while a Swedish retrospective study carried out in a large population suggests that early vaccination does not influence the onset of atopic disease in the pre-school period (12).

BCG vaccine usually induces an Th1 immune response, whereas atopic dermatitis is associated with Th2 lymphocytic infiltration. AD can be regarded as a chronic skin disease with an increased IL-4/IFN-γ ratio mediated by cutaneous lymphocyte associated antigen (CLA+) Th2 lymphocytes (13,14). Among other activities, Th2 cells produce IL-4, IL-5 and IL-10, thereby stimulating the formation of B-cells, as well as the ac-

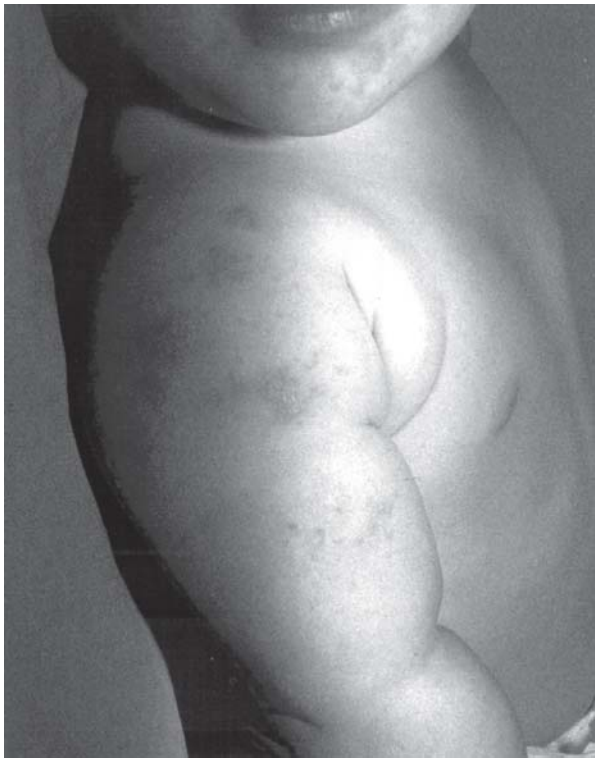

Figure 2. On the face, the right upper arm, the back, and the lower extremities, disseminated macules and papules with various diameters are present. The exanthemas were characterized by itching, reddish color, and fine scales.

cumulation of eosinophils and mastocytes in the skin.

Mycobacterium bovis BCG vaccine triggers an Th1 type of immune reaction in adults and the primary vaccination induces a similar Th1 type memory-cell response in newborns (15). In the differentiation of the activated naive Th cells, the IL-12/IL-4 ratio plays a key role. If the relative amount of IL-4 increases, the differentiation of Th2 cells will have prevalence (16).

In our patient, the genetically determined (positive family history!) relatively increased IL-4 production and in consequence the enhanced Th2 cell generation (unlike the usual Th1 immune response following BCG vaccination) can be postulated as a possible cause for the development of atopic skin symptoms. A similar mechanism is suggested by Dalton et al., upon observing the flare-up of atopic skin symptoms following BCG revaccination in two children suffering from AD (5).

Another possible mechanism may be seen in the so-called "Toll-like" receptors (TLR) found on the surface of immune as well as on endothelial cells. These receptors are capable of recognizing bacterial lipopolysaccharides and, similarly to the primary cytokine (IL-1, *TNF-α) receptors, employ the intracellular signaling system with the nuclear factor-κB (NF-κB) to trigger the transcription of genes for E-selectin (the endothelial ligand of CLA), cytokines, chemokines and adhesive molecules leading to cutaneous inflammation (17,18). Under the influence of mycobacterial cellular wall components, a subtype of TLR induces TNF-α production, which, following the previously described mechanism, may lead to inflammatory skin phenomena (19).

It is known that AD has two variants, the so-called extrinsic and intrinsic type (20). In the former, specific IgE can be detected and antiallergic therapy is effective. The intrinsic form can be characterized, by normal serum IgE levels, eosinophilia, negative immediate type skin tests, low tissue-localized IL-5 and IL-13 expression, and normal serum IL-5 levels (21).

On the basis of the normal serum IgE level and the moderate eosinophilia in our patient, the intrinsic form of AD has to be considered. The so called id-reaction is however also a diagnostic possibility. It may be assumed that BCG acts as a superantigen (SAG), causing CLA expression in T-cells, and in consequence, so-called skin homing of these cells (5).

Based on these theoretical considerations, a connection of causality between BCG vaccination and the appearance of AD symptoms may be a possibility in our patient. Renewed appearance of AD phenomena following revaccination would give substance to these speculations.

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A U T H O R S ' A D D R E S S E S

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