baseline warts (imiquimod 11% vs. vehicle 6%; p = 0.488), more imiquimod-treated patients experienced a ≥50% reduction in baseline wart area (38% vs. 14%; p = 0.013). Use of imiquimod was not associated with any changes in laboratory values, including CD4 count. It was not associated with any adverse drug-related events, and no exacerbation of HIV/AIDS was attributed to the use of imiquimod. However, it appeared that topical imiquimod was still less effective at achieving total clearance than in the studies with HIV-negative patients, which is most likely a reflection of the impaired cell-mediated immunity seen in the HIV-positive population (8).

There has also been a report of improved success when topical imiquimod was combined with more traditional destructive therapy for HPV infection in HIV-positive patients, particularly in the setting of the use of highly-active antiretroviral therapy (HAART) (9). This combination therapy appears to be increasingly more effective as viral load drops and CD4 count rises.

We believe that the case presented, particularly in the context of the studies already conducted, supports the utility of topical imiquimod for the treatment of anogenital HPV in HIV-positive individuals. Further investigation is warranted to determine the most effective regimen for its use, including the possibility of combined therapies and/or concomitant initiation of HAART.

REFERENCES


Delayed Granulomatous Lesion at the Bacillus Calmette-Guérin Vaccination Site

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Sir,

Bacillus Calmette-Guérin (BCG) vaccine is an attenuated strain of Mycobacterium bovis that was developed from a more virulent strain in 1908 at the Pasteur Institute. It has been used in many parts of the world to enhance immunity to tuberculosis (1). The available strain in Norway is from the Statens Serum Institute, produced in Denmark, which is lyophilized and is constituted of sterile diluents (without aluminium hydroxide). In Norway, BCG vaccines are routinely given to all children aged 10–13 years, by intradermal or subcutaneous injection.

BCG vaccination provides 30–80% protection against the development of tuberculosis in susceptible and appropriate populations (2). The complications occurring after BCG vaccination for tuberculosis are rare in relation to the number of vaccinations carried out. They may be local or systemic, specific or non-specific reactions. The local changes are induration, blister formation, chronic-discharging ulcer, lupus vulgaris, and regional lymphadenopathy with or without suppurrative drainage (3). The systemic reactions include erythema nodosum, erythema multiforme, generalized maculopapular eruption, exfoliative dermatitis, and papulonecrotic tuberculosis (4).

We describe a peculiar post-BCG reaction that appeared as BCG granuloma 3 years after vaccination was performed.

CASE REPORT

A 16-year-old girl presented with a simple, firm, soft, painless nodule that appeared suddenly on the left upper arm in the sulcus over the insertion of the left deltoid muscle (Fig. 1). At the site of the previous BCG vaccination given intradermally 3 years earlier, under the school health services. The present lesion was approximately 3 cm in size, bluish, and surrounded by slightly inflamed skin. The draining lymphatic glands were not palpable. The patient’s general health was good. There was no fever and weight loss. The laboratory examination was within the normal range (complete blood count, X-ray examination of the thorax, erythrocyte sedimentation rate and Pique test). There was no past or family history of tuberculosis. The biopsy specimen of the nodule showed a granulomatous infiltrate consisting of epithelioid histocytes, lymphocytes, and some Langerhans’ giant cells. There was no caseation necrosis. A special stain for acid-fast bacilli, other bacilli and fungi was negative. Cultures of the biopsy specimen were negative at 8 weeks, and polymerase chain reaction (PCR)
and did not involve other parts of the body. This localization strongly suggests a causal relationship between the BCG vaccination and the onset of this peculiar, cutaneous eruption. Because Ziehl stain, culture, and PCR mycobacterial DNA were negative, it seems that the present case represents a granulomatous reaction to proteins in the BCG vaccine and not true tuberculosis. However, the presence of tubercular bacilli has rarely been demonstrated in lesions by culture, or by DNA-PCR examination, in cases of true tuberculosis at the BCG vaccination site (8, 9).

Granulomatous reactions have been reported in cases of malignant melanoma (10–12) and other neoplasms (13) after BCG vaccine therapy, and during the course of Kawasaki disease (14). It has been postulated that molecule or molecules that are cross-reactive between suspected infectious agents and the mycobacterial BCG antigens may contribute to this inflammatory process (15).

Park et al. (16) reported lichen scrofulosorum-like eruptions localized to the previous multipuncture BCG vaccination site. The authors suspected that BCG vaccine antigens deposited in the skin together with the coexisting molluscum contagiosum in this patient could act as a trigger for a localized granulomatous reaction.

In the present case the BCG vaccination was not preceded by tuberculin skin testing or by any other vaccinations containing aluminium hydroxide used as the adsorbant, such as in diphtheria and tetanus vaccines, which may be a possible triggering factor for granulomatous formation.

The patient had not received any other vaccination at the same site, either shortly before the BCG or afterwards, at about the time of the appearance of the nodulus. The triggering factor for the localized granulomatous reaction in our patient is therefore unknown. Although local persistent lesions are not so uncommon after a BCG vaccination, this case presents an unusually large lesion that appeared after a long latency period (3 years). Treatment with curettage was effective and antituberculous therapy was not needed. Most of the localized benign complications of BCG vaccination do not require medicament treatment, but if the lesion becomes particularly troublesome, then ionization may be considered.

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Ketoprofen-induced Pemphigus-like Dermatosis: Localized Contact Pemphigus?

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Sir,

Ketoprofen is a non-steroidal anti-inflammatory drug, belonging to the group of arylpropionic derivatives, which is widely used per os and by cutaneous application as a 2.5% gel. Side-effects after oral administration mainly relate to the gastrointestinal tract and affect up to 15.3% of patients (1). Cutaneous side-effects secondary to local application are much rarer, with an estimated frequency ranging from 0.008% to 0.023% (2), depending on the commercial preparation. These consist mainly of contact dermatitis (3–6) and photocontact dermatitis (7–9), which may be persistent (10). We present herein a patient who developed a vesiculobullous dermatosis at the site of application of ketoprofen, with histologic and immunopathologic features of autoimmune pemphigus. As far as we know, contact pemphigus has never been reported before with ketoprofen.

CASE REPORT

A 65-year-old Caucasian woman had been suffering from Waldenström’s macroglobulinemia and was treated with fludarabin. Some days prior to consultation she had applied ketoprofen gel (Ketum) on her knees on two occasions to relieve arthralgia. Within a matter of hours she developed pruritic, well-demarcated, erythematous lesions over both knees, which later became studded with vesicles and small bullae (Fig. 1). On examination an additional erythematous lesion was found on the thigh. The mucous membranes were unaffected. The vesicles and bullae subsided as a result of local steroid treatment but the erythema persisted on the knees for the next 10 days. Histologic examination of a skin lesion showed a moderately acanthotic epidermis. Several deeply-seated intraepidermal vesicles were found, whose floor consisted of a single row of basal keratinocytes. The vesicles were occasionally coalescing into small blisters and contained many eosinophils (Fig. 2). The underlying dermis contained a mild inflammatory infiltrate composed of lymphocytes and eosinophils. Direct immunofluorescence performed twice on perilesional skin (at the initial consultation and 10 days later) showed deposits of IgG and C3 on the surface of epidermal keratinocytes, i.e. an aspect of autoimmune pemphigus.

Fig. 1. Well-demarcated erythematous lesion of the knee studded with vesicles and small bullae.

Fig. 2. Suprabasal intraepidermal clefting containing many eosinophils. Original magnification × 250.