Id-Like Reaction to BCG Therapy for Bladder Cancer

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Id reaction, also known as autoeczematization, is the development of dermatitis that is distant to an initial site of infection or sensitization. Clinical findings typically include an acute, intensely pruritic maculopapular or papulovesicular eruption that most frequently involves the extremities. Histology typically reveals spongiotic dermatitis that often is vesicular, and eosinophils may be present in the infiltrate. Id reactions can result from inflammatory skin conditions such as stasis dermatitis as well as infectious entities including mycobacterial infections. BCG live therapy consists of an attenuated strain of Mycobacterium bovis *that is utilized as a first-line treatment of superficial transitional cell carcinomas. We report the case of an id-like reaction in a 90-year-old man who developed an intensely pruritic, scaly, erythematous eruption on all 4 extremities 2 weeks after starting weekly intravesical use of BCG therapy for superficial transitional cell carcinoma. A representative biopsy demonstrated spongiotic dermatitis with overlying scaling and an eosinophilic infiltrate. The eruption resolved after discontinuation of BCG therapy and treatment with topical corticosteroids.*

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Case Report

A 90-year-old man presented with an intensely pruritic, scaly, erythematous eruption on all 4 extremities 2 weeks after starting weekly intravesical use of BCG live therapy for superficial transitional cell carcinoma. The lesions consisted of scaly erythematous macules and papules coalescing in some areas to form plaques (Figures 1 and 2). The eruption started 1 week after initiation of treatment and markedly intensified following the second treatment session. There was no papulovesicular component or mucosal involvement. The patient reported no history of stasis dermatitis, recent dermatophyte infection, or other infectious processes known to be associated with the development of an id reaction. His only current medication was lisinopril, which he had been taking for the last 8 years for hypertension. The patient denied any fever, chills, dysuria, cough, or shortness of breath. There was no lymphadenopathy. The patient refused further treatment with BCG therapy after the second session. The lesions were treated with betamethasone valerate cream 0.1%, which yielded complete resolution; the dermatitis recurred 1 month later but resolved from treatment with topical corticosteroids. A representative biopsy of a scaly erythematous macule on the arm demonstrated spongiotic dermatitis with overlying scaling and an eosinophilic infiltrate (Figure 3). No dermatophytes, bacteria, or bacilli were observed.

Comment

Id reaction, also known as autoeczematization, is the development of dermatitis that is distant to an initial site of infection or sensitization. Proliferation of activated T cells generally is noted, but the complete pathogenesis of the reaction remains unclear.[1] Animal models have shown that inflammatory processes of the skin, whether allergic, irritant, or infectious, lower the irritancy threshold of unaffected skin and facilitate the development of an eczematous reaction.[2,3] Histology of id reactions typically reveals spongiotic dermatitis that often is vesicular. Eosinophils are sometimes present in the infiltrate.

Whitfield[4] first described the secondary dissemination of eczema in 1921. The most common cause of id reaction is stasis dermatitis, which is often but not always associated with contact dermatitis. Id reactions also have been associated with mycobacterial, fungal, and bacterial infections.

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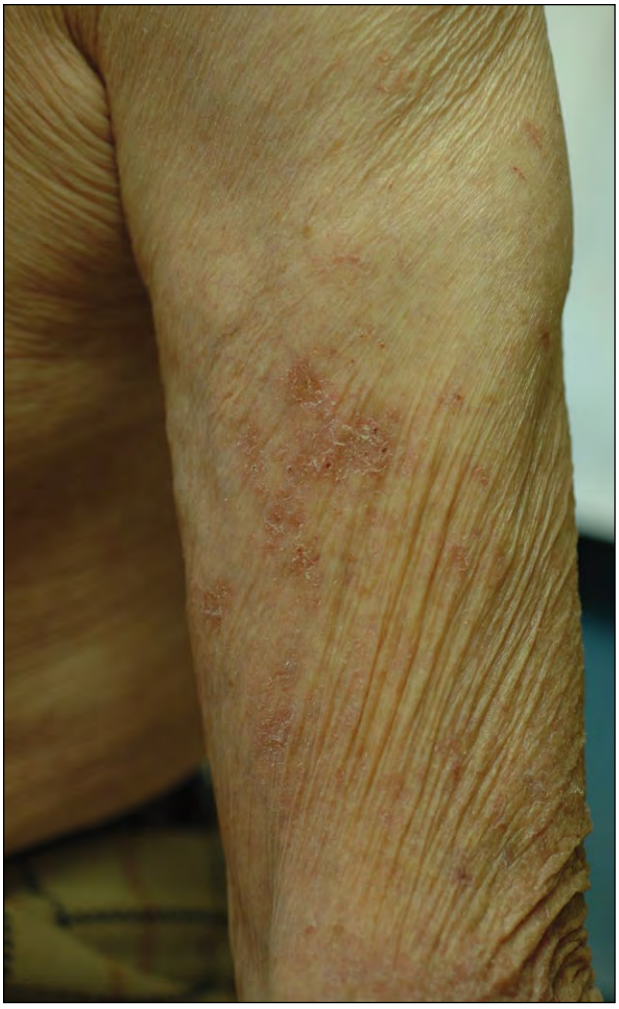

Figure 1. Scaly erythematous plaques on the left arm of a 90-year-old man undergoing BCG live therapy for bladder cancer.

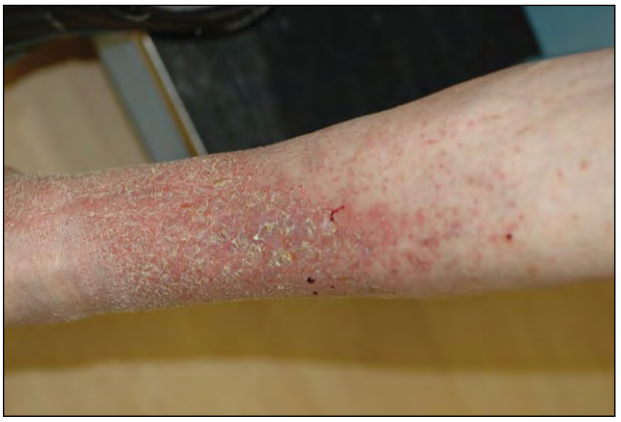

Figure 2. Scaly erythematous macules and papules coalescing to form a plaque on the left leg.

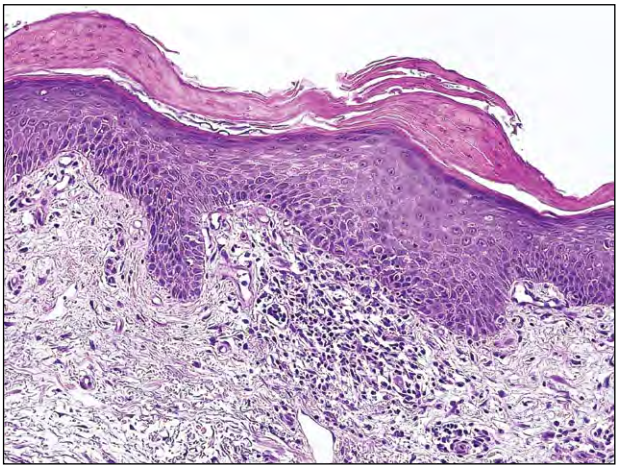

Figure 3. Spongiotic dermatitis with overlying parakeratotic scaling and scattered eosinophils within the dermis (H&E, original magnification ×40).

BCG therapy contains an attenuated strain of *Mycobacterium bovis* that consists of living bacilli, dead microorganisms, and subcellular debris. Intravesical use of BCG is considered a first-line treatment of superficial transitional cell carcinomas.[4] The incidence of urologic and systemic symptoms often increases after the third BCG treatment session as the patient's immune response peaks. Hematuria has been reported to occur in 43% of patients as well as low-grade fever in 29% of patients; systemic toxicity has been known to occur in less than 5% of patients.[5] A rare but severe complication of BCG immunotherapy is the development of disseminated bacille Calmette-Guérin disease, which includes miliary pneumonitis, granulomatous hepatitis, soft tissue infections, bone marrow involvement, and overwhelming sepsis.[5,6] As with BCG vaccination for immunization against *Mycobacterium tuberculosis* infection, cases of disseminated infection of BCG organisms also may occur with bladder instillation. A key finding associated with disseminated bacille Calmette-Guérin disease is the formation of caseating granulomas in distant organs, but detection of organisms from tissue samples can be difficult.[6]

In the largest case series documenting complications of BCG immunotherapy for superficial transitional cell carcinoma, Lamm et al[7] reported the incidence of an uncharacteristic rash in 8 of 2602 patients (0.3%); unfortunately, the investigators did not provide the specific features of these cutaneous reactions. Isolated cases of a cutaneous pityriasis rosea–like eruption and a localized necrotizing granulomatous dermatitis that failed to demonstrate mycobacterial organisms using special stains and cultures also have been reported in the literature.[8,9]

Treatment of disseminated disease arising from BCG immunotherapy typically includes isoniazid

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or other antituberculosis drugs. Oral corticosteroids generally are administered in severe cases because hypersensitivity reactions with or without actual tissue dissemination of BCG organisms are thought to play an important role in granuloma formation, clinical symptoms, and organ dysfunction.[5] Id reactions usually resolve on treatment of the localized infectious or inflammatory disorder, though recurrence is common. Topical corticosteroids and antihistamines often are effective.

Our case illustrates a previously unreported cause of a cutaneous id reaction that is associated with treatment of superficial transitional cell carcinoma by intravesical use of BCG live therapy. We present this case to raise awareness of id reaction as a diagnostic consideration in patients with superficial transitional cell carcinoma who develop skin reactions while undergoing BCG therapy, which is considered a first-line treatment of this disease.[7]

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