

Atypical Stevens-Johnson syndrome-like reaction in the setting of immune checkpoint inhibition

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ABSTRACT

Background: Stevens-Johnson syndrome (SJS) is a rare, life-threatening toxicity that has been scarcely reported among patients receiving immune checkpoint inhibitors (ICIs). There remains a poor understanding of the unusual presentation and distinguishing features of an SJS-like reaction from ICI use.

Methods: To describe the timing, clinical manifestations, and treatment course of this unusual skin toxicity, this multicenter, retrospective study identified seven patients with suspected ICI-induced SJS from January 2011 through May 2019.

Results: All seven patients (5 men; mean age, 66.6 years) presented initially as benign, limited drug eruptions after a median of 4 ICI cycles (range, 1-7) and 63 days (13-253 days) from ICI initiation. While none had prior drug allergies, all patients had received new, recently initiated – i.e., within two months – medications at the time of rash onset, including trimethoprim-sulfamethoxazole and allopurinol. All patients' benign-appearing eruptions progressed to generalized, Nikolsky-positive bullous dermatoses, and all but one developed mucosal involvement including oral (n=5), ocular (n=2), and urogenital (n=3). Cases demonstrated characteristic histologic findings of SJS, such as epidermal necrosis, and occasional atypical features, including interface dermatitis. Once suspected for SJS, all patients responded favorably to systemic therapy, primarily intravenous corticosteroids, with near immediate symptomatic resolution and cessation of progressive skin blistering or detachment. Median length of stay was 11 days and no patients died from skin toxicity.

Discussion: Our multicenter case series outlines and defines a generalized bullous eruption that mimics SJS in patients receiving ICIs, which we have termed progressive immunotherapy-related mucocutaneous eruption (PIRME). While PIRME shares some clinical and histopathological features with SJS/TEN, it is notably distinct in its delayed onset, mild initial morphological presentation, rare ocular involvement, benign clinical course, and favorable treatment response. These key differences call for a renewed exploration and sharpened understanding of this severe mucocutaneous blistering toxicity that accommodate its divergence from classic SJS. The association with concomitant medication use suggests a potential mechanism whereby ICIs reduce patient immune tolerance to subsequent drug exposures, leading to a florid exacerbation of an otherwise benign drug reaction.

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