Histopathologic Spectrum of Psoriasiform Skin Reactions Associated With Tumor Necrosis Factor-α Inhibitor Therapy. A Study of 16 Biopsies

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Abstract: Tumor necrosis factor (TNF)-α inhibitors (anti-TNF-α biologic drugs), currently used to treat different autoimmune conditions, may be associated with cutaneous drug reactions. New onset or worsening of psoriasis and psoriasis-like reactions have been reported in these patients. However, not much is known about the different histopathologic patterns of such skin lesions. The aim of this study was to evaluate the pathologic spectrum of clinically papuloussquamous to pustular “psoriasiform” lesions in this setting. Sixteen biopsies from 9 patients on anti-TNF-α therapy for rheumatoid arthritis (n = 7), Crohn disease (n = 1), and Behçet disease (n = 1) who developed a “psoriasiform” skin rash during treatment were included in this study. None of the patients had history of psoriasis. Five patients (10 biopsies) showed a psoriasis-like pattern that varied from that seen in guttate lesions (4 biopsies), to well-established plaques (3 biopsies) to pustular psoriasis (3 biopsies). Three patients (4 biopsies) showed an interface/lichenoid dermatitis mimicking lichen planus. Two patients (2 biopsies) showed features of pustular folliculitis. Eosinophils varied from none (2 biopsies) to scattered (7 biopsies) to numerous (7 biopsies). Plasma cells were present in most cases. All pustular lesions had negative cultures. In conclusion, anti-TNF drugs elicit a spectrum of cutaneous reactions that go beyond the classical eosinophilic-rich hypersensitivity reaction and may closely mimic primary dermatitis. In addition to psoriasis-like lesions, lichen plans–like dermatitis and sterile pustular folliculitis should be included in the list of anti-TNF-α–related drug reactions. Because the different histopathologic findings may be subtle, clinical correlation is crucial to make the diagnosis.

Key Words: skin, anti-TNF, psoriasis, psoriasiform, pustular, drug reaction

INTRODUCTION

Tumor necrosis factor-α (TNF-α) is a proinflammatory cytokine produced by a variety of cells including keratinocytes, Langerhans cells, and activated T lymphocytes.1,2 TNF-α is believed to play a critical role in the pathogenesis of inflammatory and autoimmune conditions such as rheumatoid arthritis, Crohn disease, and psoriasis.1,6 Thus, TNF-α inhibitors (anti-TNF-α biologic drugs) have become important agents in the treatment of such diseases. The 3 anti-TNF drugs most commonly used to treat rheumatoid arthritis and other inflammatory conditions are infliximab, adalimumab, and etanercept. Infliximab is a chimeric (three-quarters human and one-quarter mouse) anti-TNF monoclonal antibody, adalimumab is a human anti-human TNF monoclonal antibody, and etanercept is a fusion protein that links human TNF receptor 2 and the Fc component of human immunoglobulin G1.4,5 These biologic drugs bind TNF and block its access to TNF receptors on the surface of target cells, thereby preventing inflammation and tissue damage.7 However, these biologic drugs may be associated with various adverse reactions including cutaneous reactions.7–10 In addition to the paradoxical worsening of skin lesions in some patients with preexisting psoriasis, clinical lesions identical to psoriasis have been reported in patients with no personal or family history of psoriasis. Although there are reports documenting such cases,7–10 the histopathology of anti-TNF-α inhibitor–induced skin reactions remains to be characterized in a systematic fashion. The present study was conducted to determine the spectrum of histopathologic changes in patients who developed a clinically “psoriasiform” eruption while receiving anti-TNF-α inhibitors for the treatment of autoimmune diseases other than psoriasis.

MATERIALS AND METHODS

This study was approved by our Institutional Review Board. Nine patients on anti-TNF therapy for different autoimmune diseases, who developed a scaly erythematous to pustular “psoriasiform” skin eruption, were identified from the files of the Department of Dermatology, Brigham and Women’s Hospital. Subsequently, the corresponding skin biopsies were retrieved from the Department of Pathology. None of these patients had prior history of psoriasis or lichen planus. Relevant clinical data were recorded for each patient including age, sex, diagnosis, anti-TNF-α agent, clinical diagnosis of skin adverse reaction, treatment of adverse reaction, and outcome. The following histopathologic parameters were...