Calcineurin Inhibitors May Speed MF Progression

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KYOOTO, JAPAN — Topical calcineurin inhibitors should be used with caution when a diagnosis of atopic dermatitis is less than certain because they might accelerate progression of early-stage mycosis fungoides, often clinically indistinguishable from the atopic disorder. Biopsies should be obtained before initiating them on infiltrated facial lesions, which could be folliculocitic mycosis fungoides,” Grace C. Sun advised at an international investigative dermatology meeting.

Because both the symptoms and skin biopsy findings are often nonspecific in early mycosis fungoides, many affected patients are misdiagnosed as having other skin diseases—particularly atopic dermatitis—for years before the proper diagnosis is eventually made. To examine the impact of topical calcineurin inhibitor (TCI) therapy in such patients, Ms. Sun of the M.D. Anderson Cancer Center, Houston, and coworkers conducted a retrospective study of 414 M.D. Anderson patients diagnosed with stage 1A or 1B mycosis fungoides during 2001-2007.

Of the 414 patients, 27 progressed beyond their initial T1/T2 skin stage within 6 years. In a multivariate regression analysis controlling for potential confounders, three factors remained independently associated with reduced time to progression: the presence of large cell transformation on skin biopsy, which conferred a 3.3-fold increased risk of progression; prior pimecrolimus use, carrying a 4.6-fold increased risk; and dermatitic degeneration concentration, which boosted the risk of early progression 23-fold.

Twenty-one of the 414 patients had a history of pimecrolimus therapy, 4 of those 21 progressed within 6 years. So did 1 of 16 patients who had been on tacrolimus and 18 of 250 with a history of topical corticosteroid therapy prior to being diagnosed with mycosis fungoides.

Of the four patients with a history of pimecrolimus use who progressed to a more advanced T stage within 6 years after diagnosis of mycosis fungoides, three had skin biopsies consistent with folliculocitic mycosis fungoides, a more aggressive variant. Three of the four patients developed tumors in areas where they had earlier applied pimecrolimus: on the head and face in two patients with folliculocytic mycosis fungoides, and on the anecutaneous fossa and hands in another patient.

“Individually, each history of tacrolimus therapy was too small to draw any conclusions regarding a possible relationship with time to progression,” said Ms. Sun.

“Seventeen percent of the 414 patients reported being initially misdiagnosed as having eczema. Six of these 69 patients progressed within 6 years, but none had previously used a TCI, she reported at a meeting of the European Society for Dermatological Research, the Japanese Society for Investigative Dermatology, and the Society for Investigative Dermatology.

Both of the available TCIs—tacrolimus and pimecrolimus—are immunosuppressive, she said. The use of oral tacrolimus to prevent graft rejection in transplant recipients has been associated with increased risk of lymphoma; in animal models, systemic administration of either TCI has been found to increase the risk of lymphoma.