Calcineurin Inhibitors May Speed MF Progression

BY BRUCE JANCIN
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KYOTO, 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 using them on infiltrated facial lesions, which could be folliculotropic 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 emerged as being 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 5.4-fold increased risk; and a high serum lactate dehydrogenase 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 10 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 folliculotropic 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 folliculotropic mycosis fungoides, and on the antecubital fossa and hands in another patient.

The number of individuals with a 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. ■

Imiquimod Effective for Treating Squamous, Basal Cell Carcinoma

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

WILLIAMSBURG, VA. — Imiquimod can be a powerful tool for fighting in situ squamous cell carcinomas and superficial basal cell carcinomas, Dr. Roger Ceilley said.

"A number of studies have shown that imiquimod is up to 95% effective in clearing squamous cell carcinomas," said Dr. Ceilley, at the annual meeting of the American Society for Mohs Surgery. "We may worry that when treating carcinoma in situ topically, that we are just treating the tip of the iceberg, but there are a few studies now that show even patients with an early invasive squamous cell carcinoma [SCC] treated three times a week for 12 weeks show clearing of the deeper component of the lesion."

Evidence is mounting for imiquimod's use on various sites of SCC in situ, including lesions on the anterior leg and penis, said Dr. Ceilley, a professor of dermatology at the University of Iowa, Iowa City. He noted seven case reports of imiquimod used successfully to treat penile lesions. The cream was applied anywhere from twice a week to every other day, depending on individual tolerance, for 8-16 weeks. "This is clearly an off-label use and you wouldn't want to do it without consulting a urologist but, with close management, this might be an alternative for an SCC that would otherwise result in a penectomy," he said.

Combined with 5-fluorouracil, imiquimod is especially effective for SCC lesions on the scalp, and dorsum of the hand—places that are often resistant to either treatment alone.

The cream also is approved for use in superficial basal cell carcinoma, where it has shown effectiveness. A 2004 placebo-controlled study found that up to 82% of patients had histologic clearance after a 6-week treatment cycle (J. Am. Acad. Dermatol. 2004;50:722-33). The study also found no significant difference in clearance rates among patients who used the cream five or seven times a week, lending support for the shorter treatment time. However, clearance was highly correlated with increased severity of erythema, erosion, and scabbing or crusting. The cosmetic outcomes were excellent.

For BCC, Dr. Ceilley said he prefers to use imiquimod prior to Mohs surgery, in conjunction with aggressive curettage and electrodesiccation. Treating for a few weeks preoperatively can reduce the defect, decrease the frequency of residual tumor, and improve cosmetic appearance.

"You can really define the lesions more carefully, minimizing the area of surgery you have to do," he said.

'A number of studies have shown that imiquimod is up to 95% effective in clearing squamous cell carcinomas.'

DR. CEILLEY

Evidence is mounting for the use of imiquimod in nodular BCC as well—especially in smaller, low-risk lesions or as adjunctive therapy. The original 2002 dosing study found a histologic clearance rate of up to 76%, with no significant difference between those who applied the medication daily for 12 or 16 weeks (Arch. Dermatol. 2002;138:1165-71), said Dr. Ceilley.

A more recent study found that while 70 of 90 patients (78%) had a complete clinical response, there was clinically visible tumor still present in 20 patients (22%). There was complete histopathologic clearance observed in 58 patients (64%), while residual tumor remained in 32 patients (36%). Efficacy was better in lesions smaller than 1 cm in diameter. The authors concluded that, since 17% of patients in the study with clinical clearance still had pathologic evidence of disease, excisional biopsy of the treated site is still indicated (J. Am. Acad. Dermatol. 2007;57:616-21).

Dr. Ceilley stated that he did not have any conflicts of interest to disclose. ■

Weaker Lidocaine Provides Equal Pain Relief for Mohs

BY SUSAN LONDON
Contributing Writer

VANCOUVER — Compared with the lidocaine concentration typically used for local anesthesia during Mohs surgery, a lower concentration achieved equivalent pain relief with a 53% reduction in the total dose administered in a randomized, double-blind trial of 149 patients.

"We found in our clinic that 10%-15% of our patients were actually exceeding the recommended lidocaine dose of 7 mg/kg when we used 1% lidocaine with 1:100,000 epinephrine, which is the most common concentration of lidocaine used for Mohs surgery," explained Pamela Morganroth, noting that the patients nonetheless did not experience any symptoms.

"These patients often have large tumors, multiple sites, and extensive reconstructions," she said at the annual meeting of the American College of Mohs Surgery.

Minimizing lidocaine dose is important because symptoms of lidocaine toxicity occur in a dose-dependent manner; moreover, exceeding the recommended limit—even if symptoms do not occur or occur as a result of other conditions—exposes surgeons to medicolegal risk, observed Ms. Morganroth, a medical student at the University of Pennsylvania, Philadelphia.

"Unfortunately, multiple factors influence lidocaine dose," including older age; pregnancy; and renal, cardiac, and hepatic impairment, she added, "so it's virtually impossible to set a uniform maximum recommended lidocaine dose."

In the study, patients undergoing Mohs surgery were randomly assigned to local anesthesia consisting of 1.0% lidocaine with 1:100,000 epinephrine or 0.5% lidocaine with 1:200,000 epinephrine. Surgery was performed by a single physician who was unaware of the patient's assignment. The surgical field was infiltrated immediately before each Mohs layer and the reconstruction, with use of local infiltration and field blocks instead of regional nerve blocks. Excision began as soon as the patient reported no pain to a pinprick stimulus.

Outcomes included the total lidocaine dose administered (including all stages of Mohs surgery and the reconstruction) and patient comfort, which was measured subjectively with a 100-mm visual analog scale and objectively according to the volume of "rescue" lidocaine administered during the surgery. Analyses were based on 74 patients (with 83 tumors) in the 1.0% lidocaine group and 75 patients (with 85 tumors) in the 0.5% lidocaine group.

The mean total dose of lidocaine administered to patients in the 0.5% group was significantly lower, by 53%, than that administered to patients in the 1.0% group (139 mg vs. 297 mg). Mean scores for patient-rated pain (3.88 vs. 3.11 mm, respectively) or mean volume of rescue lidocaine administered (0.85 vs. 0.33 cc) did not differ significantly, Ms. Morganroth reported.

It appears that "0.5% lidocaine provides equivalent patient comfort at half the total dose of lidocaine as compared to 1.0% lidocaine," she said, while also acknowledging that the study did not measure blood levels of the drug.

"Our study demonstrates that 0.5% lidocaine decreases the risk of dose-dependent lidocaine toxicity without compromising patient comfort during Mohs surgery," said Ms. Morganroth, who reported having no conflicts of interest. ■