EXPERT OPINION

Don't Cede Early-Stage Mycosis Fungoides

BY JOAN GUITART, M.D.

Early stages of mycosis fungoides should be managed by dermatologists, not ceded to oncologists, as often happens. I would hate to see our great specialty demoted to the treatment of acne warts and cosmetic conditions. Let's not give away this disease, too. It belongs to us.

Especially early on, there's a very important role for skin-directed therapy—and we dermatologists are the experts, not the oncologists.

Abundant evidence shows that pathogenetic events leading to tumor progression in myosis fungoides (MF) occur in the skin, and that skin-directed therapy can induce prolonged remissions.

That's a point particularly worth emphasizing in light of the European Organisation for Research and Treatment of Cancer's current recommendation that "expectant management" is a legitimate option in patients with stage IA disease because they have a normal life expectancy. This recommendation is based on a misinterpretation of the data. What the guideline writers failed to realize is that these stage IA MF patients in the major reported series who are doing so well are actually receiving skin-directed treatment. We really don't have good data on the natural history of mycosis fungoides without treatment, so their conclusions are based on faulty information.

Patients with cutaneous T-cell lymphoma (CTCL) face numerous problems in which dermatologists have special expertise: severe pruritus, xerosis, cosmetic issues, an increase in skin cancers, and numerous cutaneous infectious complications.

In one study of 356 patients with MF or Sézary syndrome, the incidence of cutaneous bacterial infection was 17% per year (JAMA 1992;267:1354-8). The combined annual rate of cutaneous herpes simplex and herpes zoster infections was 3.8%. Extracutaneous CTCL involvement independently predicted a 12-fold increased risk of recurrent bacterial skin infection, a 28-fold increase in disseminated herpesvirus infection, and a rather remarkable 15-fold increase in death from infection.

We, as dermatologists, are very well qualified to manage these infections.

A study recently completed at Northwestern University in Chicago showed roughly a 40% *Staphylococcus aureus* colonization rate in CTCL patients. Worsening of the skin lesions or a new flare of erythroderma in CTCL patients may be related to a cutaneous infection rather than tumor progression.

At Northwestern, we recommend culturing patients often and utilizing frequent dilute bleach baths to help control *S. aureus* colonization levels. That's important because *S. aureus* superantigen has been shown to stimulate tumor-infiltrating lymphocytes, thus encouraging growth of malignant T cells. Treating a concurrent *S. aureus* skin infection may be sufficient to curtain a Sézary syndrome crisis, for example.

The quality of life issues raised by CTCL are often striking and here again dermatologists can be uniquely helpful. A survey of the Mycosis Fungoides Foundation membership found that 62% of respondents indicated their disease made them feel unattractive. A profound distress over health concerns was nearly universal (Cancer 2006;107:2504-11).

With skin-directed therapies, it is important to apply agents such as topical steroids, nitrogen mustard, and retinoids not only to the actual lesions but for a few centimeters beyond the actual clinical borders. Oncologists generally handle systemic therapies for CTCL, but there has been considerable interest among dermatologists in vorinostat (Zolinza), an oral inhibitor of histone deacetylase (HDAC) approved by the Food and Drug Administration in 2006 for the treatment of CTCL.

I have been less than favorably impressed by the low response rates—24% and 30% in two published trials—as well as the short duration of response and extensive side effects. In general, I think dermatologists feel comfortable prescribing oral treatment, but I would recommend caution on its use. The risk-benefit ratio is not that great, and in any case new HDACs with perhaps a better safety profile and efficacy are in the pipeline.

Dermatology has lost control of too many important diseases like sexually transmitted diseases, connective vascular conditions, and other allergy/immunology conditions. We should not lose track of mycosis fungoides, too. ■

DR. GUITART *is professor of dermatology at Northwestern University. He disclosed being a consultant to Ligand Pharmaceuticals Inc.*

Add Points for Mycosis Fungoides Dx

BY BRUCE JANCIN
Denver Bureau

WAIKOLOA, HAWAII — The standardized, points-based diagnostic algorithm for early mycosis fungoides developed by the International Society for Cutaneous Lymphoma can be helpful in approaching the ambiguous patient with a patchy, thin-plaque rash and some atypia in the biopsy, Dr. Kimberly Bohjanen said at the annual Hawaii dermatology seminar sponsored by Skin Disease Education Foundation.

In the past, such a patient might visit four different physicians and variously receive a diagnosis of parapsoriasis, atopic dermatitis, contact dermatitis, or early classic cutaneous T-cell lymphoma (CTCL), noted Dr. Bohjanen of the University of Minnesota, Minneapolis.

Although the algorithm—co-developed by the Cutaneous Lymphoma Task Force of the European Organisation for Research and Treatment of Cancer—might seem confusing at first, it really is not. In fact, it's akin to the scoring system rheumatologists developed to define systemic lupus, she said.

Four points are required to diagnose early mycosis fungoides. Up to two can come from the clinical exam. The basic clinical criterion is the presence of persistent and/or progressive patches and thin plaques. The additional clinical criteria are a non–sun-exposed "bathing suit"–type lesion distribution, poikiloderma, and variation in lesion size and shape. A patient gets one point for presenting with the basic clinical criterion plus one of the additional criteria, or two points for presenting with the basic criterion plus any two additional clinical criteria.

Up to two points can be awarded based on the histopathologic findings on biopsy.

The basic histopathologic criterion is the presence of a superficial lymphoid infiltrate. If this, plus either of the two additional criteria—epidermotropism without spongiosis, and lymphoid atypia as defined by enlarged, irregular, hyperchromatic nuclei—are met, that's worth one point. If the basic and both additional criteria are present, that's worth two points.

"So basically if you have someone with a classic presentation of CTCL that meets the criteria on clinical exam and then you have a biopsy with all of these features, you've made the diagnosis of CTCL without even going on to immunotyping or T-cell gene rearrangement," she said.

All of this presupposes that the possibility of drug eruption has been ruled out from the outset.

A subsequent biopsy is used to gather material for T-cell gene rearrangement and immunopathologic studies. These studies need to be done routinely because of their value in staging, even in patients who already have four points.

One additional point is awarded for evidence of clonality on T-cell gene rearrangement. The algorithm gives another point if at least one of the following three immunopathologic markers of CTCL is present on the cell surface: less than 50% CD2-positive, CD3-positive, or CD5-positive T cells; less than 10% CD7-positive T cells; and discordance between the epidermal and dermal population of CD2, CD3, CD5, or CD7 T cells, with the antigen deficiency being confined to the epidermis (J. Am. Acad. Dermatol. 2005;53:1053-63).

The new system follows the T (tumor), N (lymph nodes), M (visceral metastases), and B (blood—with or without circulating Sézary cells) format (Blood 2007;110:1713-22). The biggest change was in lymph node staging, which now incorporates clonality, she said.

Dr. Bohjanen disclosed being on the speakers bureau for Abbott Laboratories.

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Unifying Term Proposed for T-Cell Clonality Diseases

WAIKOLOA, HAWAII — The phrase "cutaneous T-cell lymphoid dyscrasia" could serve as a novel unifying term for a variety of chronic skin conditions characterized by persistent T-cell clonality without meeting the histologic or clinical criteria for mycosis fungoides, Dr. Joan Guitart proposed at the annual Hawaii dermatology seminar sponsored by Skin Disease Education Foundation.

Cutaneous T-cell lymphoid dyscrasias encompass eight distinct clinicopathologic precancerous entities, and is a better term than "precutaneous T-cell lymphoma" or "premycotic" because most affected patients will in fact have an innocuous, indolent clinical course without ever progressing to overt cutaneous T-cell lymphoma (Arch. Dermatol. 2007;143:921-32).

For example, long-term studies demonstrate that only 10%-15% of patients with parapsoriasis—one form of cutaneous T-cell lymphoid dyscrasia—evolve into mycosis fungoides, explained Dr. Guitart, professor of dermatology at Northwestern University, Chicago. He proposed the following criteria as requisite for cutaneous T-cell lymphoid dyscrasia:

- ► The condition is chronic with a tendency to relapse following topical therapy.
- ► There is no known triggering event, such as the occurrence of T-cell clones in conjunction with rheumatoid arthritis, lupus erythematosus, organ transplants, or other states of long-term immunostimulation. There also is no evidence of allergic reaction, hypersensitivity, or connective-tissue disorder.
- ► There is the presence of one or a few T-cell clones defined by reduced CD7 and CD62L expression in skin specimens.
- ► There is a lack of morphologic evidence for T-cell lymphoma. The dominant lymphocyte is small or intermediate in size.

Other skin disorders fitting the definition include pityriasis lichenoides chronica, idiopathic follicular mucinosis, atypical lymphocytic lobular panniculitis, clonal erythroderma, pigmented purpuric variant, syringolymphoid hyperplasia with alopecia, and hypopigmented interface variant.

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—Bruce Jancin