Mycosis Fungoides Appears Early in Black Women

BY BRUCE JANCIN

SAN FRANCISCO — Mycosis fungoides is classically considered a disease of middle-aged white men, but onset prior to age 40 years is significantly more common in black women than in white men or women, according to the experience at M.D. Anderson Cancer Center.

Moreover, young black women with mycosis fungoides (MF) are particularly likely to have rapid progression with a poor prognosis, Patricia Sun reported at the annual meeting of the American Academy of Dermatology.

"We would like people to consider more aggressive therapy in African American women who present with MF before age 40—including allogeneic transplantation—earlier than you would think of it in other patients," said Ms. Sun of M.D. Anderson and the University of Texas, Houston.

MF is the most common form of cutaneous T-cell lymphoma, with an annual incidence of 6.4 cases per million population. The peak age at presentation is 60-69 years. The ratio of men to women with MF is roughly 2:1. The disease is most often characterized by an indolent course, and in one large series, median survival was 10 years. MF is more common in whites than blacks.

However, when the cutaneous T-cell lymphoma team at M.D. Anderson recently noticed a small cluster of young black women who presented with MF of an aggressive nature, it enlisted Ms. Sun to lead a study aimed at learning whether these cases were simply a fluke or were representative of a consistent yet previously unrecognized trend.

Ms. Sun analyzed the prospectively collected data on 1,074 MF patients who presented to the cancer center during 1969-2007. She noted onset prior to age 40 years in 33% of black patients, 36% of Hispanics, and 13% of whites. Women presented with MF prior to age 40 significantly more often than did men. Indeed, 35% of the 40 black women with MF in the series presented before age 40, as did 48% of 40 affected Hispanic women and less than 15% of 550 white women.

Aggressive disease—defined as rapid progression from stable, mild disease to stage IV in the span of less than a year at any time during the disease course—occurred in nine women with early-onset MF. Eight of these women were black and one was white. Six of the eight black women with aggressive early-onset MF died of their disease; the two survivors underwent allogeneic transplantation.

Why the poorer outcome in black women with MF before the age of 40? "Our thought is vitamin D," Ms. Sun said. "I know everybody's talking about vitamin D now, but many of our African American patients are vitamin-D deficient."

One audience member cautioned that MF is notoriously difficult to diagnose, particularly in darker-skinned individuals, and there's probably a bias for the more severe cases to be referred to M.D. Anderson. ■

New Primary Cutaneous B-Cell Lymphoma Guidelines Highlight Differential Diagnosis

BY DAMIAN McNAMARA

HOLLYWOOD, FLA. — The differential diagnosis and management of primary cutaneous lymphoma rely to a great extent on whether lesions appear on the leg or elsewhere, according to the first guidelines released by the National Comprehensive Cancer Network.

"Diffuse B-cell lymphoma on the leg often leads to death," Dr. Steven M. Horwitz said. In contrast, other forms of primary cutaneous lymphoma, including follicle center and marginal zone disease, generally are indolent, and a majority of patients survive a decade or more after diagnosis.

"One of the questions is: Why have a guideline? Why not just treat this like other lymphomas?" Dr. Horwitz said at the annual conference of the National Comprehensive Cancer Network (NCCN). "A take-home point is there are notable differences between cutaneous B-cell lymphomas that affect treatment."

The genesis of the first guidelines was an observational study that found 5-year survival was 94% for non–leg-type cutaneous lymphoma patients versus 52% for leg-type disease (J. Clin. Oncol. 2001;19:3602-10). "Keep in mind the leg patients tend to be older," Dr. Horwitz said. Another study by the European Organization for Research and Treatment of Cancer (EORTC) confirmed this overall survival disparity out to 11 years (Curr. Opin. Oncol. 2006;18:425-31).

Clinical presentation, pathology, imaging, and "more and more" immunophenotyping can aid diagnosis, he said. For example, primary cutaneous follicle center lymphoma (FCL) is more common than the deadlier primary cutaneous diffuse large B-cell lymphoma (DLBCL), leg type. "In lymphoma we are not shy about giving things really long names," said Dr. Horwitz of Memorial Sloan-Kettering Cancer Center, New York.

FCL is typically an erythematous nodule with smooth skin on top. "And it doesn't have to be a small lesion, even though it's indolent," Dr. Horwitz said. In addition, FCL has a predilection for the scalp and forehead and tends to grow slowly and spontaneously regress.

In contrast, DLBCL leg-type is associated with rapid growth and features frequent mitosis. "But be a little careful. It could be a pseudolymphoma. Just a high proliferation rate only does not automatically mean leg disease," said Dr. Horwitz.

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DR. HORWITZ

Histopathology differences are outlined in the guidelines. It is essential that a pathologist with expertise in diagnosis of primary cutaneous B-cell lymphoma review all tumor slides. A punch, incisional, or excisional biopsy is recommended. "Shave biopsies we don't like because the infiltrate is dermal," said Dr. Horwitz, a member of the NCCN panel that developed the guidelines.

Also essential to differential diagnosis is an immunophenotyping panel. For example, "A CD5 positive result means it is probably a skin manifestation of a systemic lymphoma," Dr. Horwitz said. Primary cutaneous lymphoma is a definition of exclusion, diagnosed when there is no evidence of extracutaneous disease on complete staging with physical examination, CT, bone marrow biopsy, and/or PET scan.

Diagnostic methods "useful in certain circumstances" include peripheral blood flow cytometry, molecular genetic testing for antigen receptor gene rearrangements, and cytogenetics or fluorescent in situ hybridization assays.

Work-up is also divided into essential and sometimes useful strategies. Complete history and physical examination, including a complete skin exam, are essential, for example. "I know it slows you down, but you really want to get patients to take all their clothes off and look at all of their skin. Even ask them to take their socks off and examine their feet," Dr. Horwitz said.

Order a complete blood count with differential, comprehensive metabolic panel, lactase dehydrogenase assay, and test for hepatitis B, if treatment includes rituximab (Rituxan, Genenetch).

Essential imaging includes a chest/abdominal/pelvic CT scan. A PET-CT scan is useful in certain circumstances. Dr. Horwitz said, "If you really think the person has local disease, PET is probably better for finding evidence of extracutaneous disease."

A bone marrow biopsy is considered essential with DLBCL, leg type. It also is useful for patients with FCL but is optional if the patient has marginal zone lymphoma (MZL), the other major form of indolent primary cutaneous disease.

The NCCN guidelines include a section to identify appropriate candidates for localized radiation therapy. Solitary skin involvement, regional disease, and systemic disease are differentiated according to clinical judgment. For solitary or regional T1-T2 FCL and MZL disease, for example, "almost all patients will respond" to locoregional radiation therapy or excision, he said.

Dr. Horwitz is a consultant for Eisai, Genenetch Inc., Merck & Co., and Therakos. He also is on the speakers bureau for Merck and receives grant and research support from Allos Therapeutics, Genzyme Corp., and Gloucester Pharmaceuticals. ■

Predictors Are Needed

SLN *from page 1*

studies that included recurrence and/or survival data, there were four deaths among SLN-positive patients and an equal number among SLN-negative patients. Melanoma recurred in five SLN-positive and nine SLN-negative patients.

American Joint Committee on Cancer guidelines recommend SLN biopsy in patients with melanomas 1-4 mm thick, but as a result of improved screening, nearly 70% of all melanomas are diagnosed as thin lesions. The indications for SLN biopsy aren't well defined for patients with thin melanomas, yet the procedure is increasingly being applied in this setting, Dr. Warycha noted.

She and her coinvestigators combed the studies included in their meta-analysis for clinical and histopathologic features that might reliably identify those patients with thin melanoma who were more likely to be SLN positive. Unfortunately, no such predictors emerged. Ulceration, Clark's level, tumor regression or lack thereof, vertical growth phase—none proved to be significantly associated with SLN positivity.

Mitotic index showed a positive signal in a University of Pennsylvania study of 181 thin melanomas in which a mitotic rate greater than 0 was associated with a SLN positivity rate of 12%, as compared with 5% with a mitotic rate of 0 (Ann. Surg. Oncol. 2005;12:449-58). This relationship, however, was not confirmed in the other studies.

Reliable predictors of SLN positivity in patients with thin melanoma are urgently needed, Dr. Warycha emphasized. The poster version of her talk won first place out of roughly 800 entries in the annual AAD poster competition. ■