A Look at New Developments in Cutaneous T-cell Lymphoma

Recent research has identified prognostic indicators and a promising treatment option for a disease that is often a significant management challenge.

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Cutaneous T-cell Lymphoma (CTCL) can represent a significant management challenge. Despite the lack of a perfect intervention, in many instances it is possible to successfully control the disease and even induce remission. This is the case even in late stage disease. Of course, prognosis is best for patients diagnosed early in the course of the disease, so accurate diagnosis is critical. The following is an update on recent developments regarding the diagnosis and treatment of CTCL.

Prognostic Indicators

CTCL generally occurs in individuals over age 40 and is most prevalent in those over age 70. But the disease can occur in younger individuals, including those under age 16. Recent data suggest that the prognosis can be good for juvenile patients. Previous studies have looked at juvenile CTCL, but only recently have we seen data from the largest series of patients under age 16. Published in *Cancer,*[1] the retrospective analysis found that disease-specific survival rates among the studied individuals at five and 10 years were 95 percent and 93 percent, respectively. Disease progression rates were five percent and 29 percent at five and 10 years, respectively. The outlook apparently is best for individuals with Stage IA disease as well as those with hypopigmented or poikilodermatous lesions and those with associated lymphatoid papulosis. Subgroup analysis found patients with these characteristics demonstrated improved disease-specific survival and reduced disease progression compared to others.

Because mycosis fungoides varies widely in symptoms and outcome and disease progression can vary widely (disease can by stable and limited to skin with no morbidity, or it can be progressive leading to death), there is significant interest in identifying prognostic indicators. In adults, high blood eosinophil absolute counts at baseline may indicate a poor prognosis for individuals diagnosed with primary CTCL. Researchers recently attempted to determine the prognostic value of various initial characteristics in patients with primary cutaneous T-cell lymphoma.[2] In univariable analysis, they found significant prognostic value for diagnosis according to European Organization for Research and Treatment of Cancer (EORTC) classi-

The Importance of Early Diagnosis

All current interventions are most effective when implemented early in the disease course. Diagnosis of CTCL is often difficult, but dermatologists must be vigilant for signs and symptoms. Dermatologists should:

- Note that many but not all patients develop classic psoriasisiform lesions.
- Be suspicious when patients present with diffuse erythema of unknown origin and/or persistent non-pruritic rash.
- Biopsy areas of persistent diffuse erythema of unknown origin and/or persistent non-pruritic rash.
- If biopsy does not reveal a cause of erythema or rash, continue serial biopsies every six (preferred) to 12 months.
- Recall that additional indicators of CTCL include abnormal white blood cell count and differential, elevated LDH levels, and circulating Sezary cells.
- Refer patients with suspected CTCL to specialists who will use molecularly-based diagnostic tests to confirm the diagnosis and provide staging.

fication, type of skin involvement, raised blood eosinophil absolute count, and raised serum level of lactate dehydrogenase, but not for age and sex. Significant prognostic factors for disease-specific death were EORTC classification and a raised blood eosinophil absolute count. Multivariate analysis found that only blood eosinophilia was associated with disease progression and disease-specific death.

Most recently, a study looked at 55 patients with mycocis fungoides over a 16 year period in an attempt to identify prognostic attributes.[3] They report that tumors (skin stage T3) or erythroderma (T4) were the most powerful predictors of poor outcome. Additionally, detection of clonality by PCR did not prove to be a stronger predictor than clinical staging, although some studies have shown value for this test suggesting poor prognosis when positive.

Treatment Options

For patients with more advanced disease, treatment often falls to a tertiary care center, specialist treatment center, or University-based clinic. However, dermatologists may treat less advanced disease, commonly employing phototherapy or topical therapies. Phototherapy has been shown to halt progression and in some cases improve CTCL. Bexarotene (Targretin, Ligand) is a common topical intervention. Often called a "rexinoid," the agent binds the retinoid X receptors and shows promise as a twice-daily treatment for CTCL.

Recent data suggest that the combination of phototherapy and oral bexarotene may be a safe and effective treatment option that may warrant consideration by dermatologists in the clinic. Retrospective chart review analysis included eight patients with CTCL (stage Ia to IIb) who had failed multiple single-agent treatment regimens (including electron-beam irradiation, interferon, PUVA, and topical steroids) and were subsequently treated with PUVA in combination with low-dose oral bexarotene.[4] All eight patients demonstrated initial response, and five achieved complete remission. The most common adverse event was pruritus. The authors concluded that the "good safety profile" associated with the combination approach warrants its consideration for patients with treatment-resistant CTCL.

More advanced treatment options for CTCL likely to be administered by specialty clinics include mechlorethamine hydrochloride (Mustragen) and carmustine (BCNU). Photopherisis is another treatment option that, combined with proper therapies in appropriately selected patients, is quite promising. Finally, IFN-alpha1a, IL-2 and IL-12, and total-skin electron-beam radiotherapy (TSEBT) are advanced options that continue to show promise and are under study.

New in Your Practice

Mela-no-more? Based on positive results of a Phase 3 clinical trial, Antigenics, Inc, anticipates FDA approval for its new Stage IV Melanoma drug, Oncophage. Data show that in all randomized stage IV Melanoma patients, median survival, improved by more than 50 percent in the Oncophage-treated arm compared with those in the physician's choice treatment arm—20.9 months versus 12.8 months. According to Antigenics, this is the first phase 3 randomized trial of a cancer vaccine to show a potential survival benefit in this category of melanoma patients.

Family Matters. Familial and non-familial melanomas may not be all that different after all. A recent study in the Journal of Clinical Oncology (23: 7168- 7177 examined data on more than 2,659 cases with family history information. Individuals in the top nine percent had high familial risk and the remainder a low familial risk. In the high familial risk group, the age at first diagnosis of melanoma was 57 years, slightly lower than in the low risk group age of 60 years. Additionally, 12 percent of the high-risk group had melanomas diagnosed by the age of 30 compared with those in the low-risk group at 6 percent.

Filtering Away Fibrosis. According to a recent study in Public Library of Science Medicine (2: e354), low doses of paclitaxel (Taxol) greatly reduce fibrosis in scleroderma skin grafts in animal models, leading to much less collagen production in the skin of treated subjects than in untreated controls. Due to the positive results, researchers study is now plan a clinical trial to test the effects of low-dose Taxol in scleroderma patients.

Showing Promise

Despite the gravity of the diagnosis of CTCL for some patients, many individuals have a good prognosis and may even achieve clearance. Dermatologists play a critical role in identifying the disease early in its course and managing and supporting patients throughout treatment. Recent developments prove that there is great promise for patients with CTCL, and research continues into alternative and potentially more effective treatments.

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