Evaluation, Diagnosis, and Staging of Cutaneous Lymphoma

Elise A. Olsen, MD

KEYWORDS

• Primary cutaneous lymphoma (PCL) • Cutaneous T-cell lymphoma (CTCL)
• Cutaneous B-cell lymphoma (CBCL) • Mycosis fungoides • Sézary syndrome

KEY POINTS

- The unique features of the diagnosis, evaluation, classification and staging of mycosis fungoides and Sézary syndrome.
- The evaluation, classification and staging of the nonMF/nonSS CTCLs and the most common subtypes of CBCLs.
- The response criteria for evaluation of therapeutic efficacy for all subtypes of cutaneous lymphoma.

INTRODUCTION

Cutaneous lymphomas are an extremely heterogeneous group of non-Hodgkin lymphomas (NHLs) that manifest in the skin.[1,2] Although most patients do not have evidence by traditional screening methods of extracutaneous disease at the time of presentation (and, hence, fit the classic definition of primary cutaneous lymphoma [PCL]), those with certain clinical or histologic subtypes commonly have, or will, develop nodal, visceral, and/or blood involvement. The prognosis and survival of patients varies not only on the type of cutaneous lymphoma but the stage as well; each lymphoma has its own best treatments to date, which are primarily stage based. Because there is no cure for any of these cutaneous lymphomas, but treatment can be life saving and insure quality of life, the overall prognosis for any given patient begins with the correct diagnosis and staging. It is the purpose of this article to discuss the evaluation, diagnosis, and staging of the 3 main subcategories of cutaneous lymphoma.

SUBTYPES AND EPIDEMIOLOGY OF CUTANEOUS LYMPHOMA

The annual incidence of PCLs is estimated at 10.0 to 10.7 per million person-years,[3,4] and they account for 19% of cases of extranodal lymphomas.[4] The World Health Organization–European Organization for Research and Treatment of Cancer (WHO-EORTC) have classified the cutaneous lymphomas with primary cutaneous manifestations into cutaneous T-cell lymphomas (CTCLs) and cutaneous B-cell lymphomas (CBCLs) (**Box 1**).[5,6] The CBCLs are the least common of the PCLs, estimated at 3.1 per million person-years in an assessment of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registry for 2001 to 2005 but making up 29% of all PCLs.[4] The annual incidence rate of CBCLs steadily increased to an annual rate of 3.92 between 2006 and 2010.[7] The age-adjusted incidence of all types of CTCLs, based on 2 different sets of SEER, ranged from 6.4 to 7.7 million person-years.[4,8] What is clear is that the incidence

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Department of Dermatology, Trent & Erwin Roads, Duke University Medical Center, Durham, NC 27710, USA
E-mail address: elise.olsen@dm.duke.edu

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Box 1
WHO/EORTC classification of cutaneous lymphomas

CTCLs and cutaneous NK-cell lymphomas

- Mycosis fungoides (MF)
- MF variants and subtypes
  - Folliculotropic MF
  - Pagetoid reticulosis
  - Granulomatous slack skin
- Sézary syndrome
- Adult T-cell leukemia/lymphoma
- Primary cutaneous CD30+ lymphoproliferative disorders
  - Primary cutaneous anaplastic large cell lymphoma
  - Lymphomatoid papulosis
- Subcutaneous panniculitis-like T-cell lymphoma
- Extranodal NK/T-cell lymphoma, nasal type
- Primary cutaneous peripheral T-cell lymphoma, unspecified
  - Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (provisional)
- Cutaneous γ/δ T-cell lymphoma
- Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoproliferative disorder (provisional)
- Primary cutaneous acral CD8+ T cell lymphoma (provisional)

CBCLs

- Primary cutaneous marginal zone lymphoma
- Primary cutaneous follicle center lymphoma
- Primary cutaneous diffuse large B-cell lymphoma, leg type
- Primary cutaneous diffuse large B-cell lymphoma, other
  - Intravascular large B-cell lymphoma
  - EBV+diffuse large B-cell lymphoma of the elderly (provisional)

Precursor hematologic neoplasm

- Blastic plasmacytoid dendritic cell neoplasm

Abbreviations: MF, mycosis fungoides; NK, natural killer.

Adapted from Willemze R, Jaffe E, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. Blood 2005;105:3769; with permission.

of both CBCLs and CTCLs has continued to increase dramatically and consistently over the past 3 decades,[4] CTCL by 2.9 per million per decade.[8] Based on the numbers available, there are over 3000 new patients with the diagnosis of PCL each year.

Mycosis fungoides (MF) is the most common type of CTCL, comprising 53–54%[4,9] to 73%[8] of cases of CTCL in various SEER reviews. Sézary syndrome (SS) is classified as a separate entity from MF by the WHO-EORTC[10] but shares the same histologic criteria and staging as MF and often evolves from MF.[1] SS accounted for 2.5% of the cases of CTCL in the report by Criscione and Weinstock.[8] The prevalence of MF is likely more than 50,000 based on survival curves, but this number is unsubstantiated without a formal registry. The 10-year survival of patients with MF with tumor or nodal involvement is compromised (42% and 20% respectively),[5] and the 5-year survival of patients with SS (who have blood and may also have node involvement) is 24% in one report.[5] Although these patients with tumor or node stage MF or leukemic blood involvement are the minority of patients with MF, they represent the potential progression for which treatments used in those with lesser disease strive to prevent. There is no current cure for MF or SS; patients living with MF or SS endure the chronic symptoms and signs of their disease and the constant time, cost, and potential side effects of treatment to prevent progression. Although there are general clinical characteristics, such as skin (T) stage, or histologic features, such as large cell transformation (LCT), that are able to identify those with a worse prognosis in certain situations, there is great heterogeneity in these subclasses of PCL and no treatment available that targets the trigger for the final unremitting growth of the lymphoma that occurs in some patients. In addition, no genetic markers are currently available that would help identify subsets of patients more likely to respond to certain treatments.

Short of a long-term national registry of patients with cutaneous lymphoma and clear documentation of the effect on overall prognosis and survival of the various treatments used and the potential for clinical, histologic, and genetic factors to influence the outcome or choice of treatment, physicians are unable to make the kind of advances necessary to move toward a curative treatment of MF and SS. The same issues are present in the other types of CTCLs and CBCLs, none of which currently have curative treatment and, because of their relative small numbers, would benefit greatly from a national registry.