Sézary syndrome: A study of 176 patients at Mayo Clinic

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Background: Sézary syndrome (SS), a leukemic variant of cutaneous T-cell lymphoma, is characterized by erythroderma and by atypical lymphocytes (Sézary cells) in peripheral blood. Although numerous studies have examined the range of disease in cutaneous T-cell lymphoma, a relative paucity of data exists to describe the long-term outcome of patients with SS.

Objective: We sought to study long-term survival and prognostic factors of patients with SS.

Methods: A retrospective chart review was conducted to identify patients with SS seen at Mayo Clinic from 1976 to 2010. Cox proportional hazards regression models, adjusted for age, were fit to evaluate factors associated with overall survival.

Results: In total, 176 patients were identified with a clinicopathologic diagnosis of SS. Overall survival was 86.1% and 42.3% at 1 and 5 years, respectively, after diagnosis (median survival, 4.0 years). After adjustment for age, potential predictors of worse survival included lactate dehydrogenase level at presentation (hazard ratio [HR] 1.71; 95% confidence interval [CI] 1.18-2.47 per doubling), prior diagnosis of mycosis fungoides (HR 2.68; 95% CI 1.44-4.98), and the presence of T-cell receptor gene rearrangements in skin (HR 2.59; 95% CI 1.38-4.87) and in blood (HR 2.05; 95% CI 1.00-4.21).

Limitations: This study is retrospective and represents a single academic center population.

Conclusions: To our knowledge, this research evaluated the largest population of patients with SS studied to date. It shows that overall survival continues to be poor, with a median survival of 4.0 years after diagnosis. (J Am Acad Dermatol 2012;67:1189-99.)

Key words: cutaneous T-cell lymphoma; outcomes assessment; prognosis; Sézary syndrome; survival.

Sézary syndrome (SS) is a leukemic variant of cutaneous T-cell lymphoma (CTCL) that arises from skin-homing lymphocytes. It is characterized by erythroderma, keratoderma, lymphadenopathy, and the presence of atypical lymphocytes with cerebriform nuclei (Sézary cells) in peripheral blood.[1-5] Over the past several decades, the diagnosis of SS has undergone progressive revisions, with the most recent diagnostic criteria proposed in 2007 by the International Society for Cutaneous Lymphomas (ISCL)/European Organization for Research and Treatment of Cancer (EORTC) and

Abbreviations used:

CI:	confidence interval
CTCL:	cutaneous T-cell lymphoma
EORTC:	European Organization for Research and Treatment of Cancer
HR:	hazard ratio
IQR:	interquartile range
ISCL:	International Society for Cutaneous Lymphomas
LDH:	lactate dehydrogenase
MF:	mycosis fungoides
SS:	Sézary syndrome
TCR:	T-cell receptor

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including immunophenotyping and molecular criteria, in an effort to better distinguish SS from mycosis fungoides (MF) and other erythrodermic CTCLs.[6,7] These criteria updated the 1979 National Cancer Institute and MF Cooperative Group TNM(B) staging classification system that was previously used to define MF and SS, and increased emphasis was placed on defining the degree of peripheral blood involvement in establishing a diagnosis.[6] Recognizing the clinical challenges in defining SS and separating it from other erythrodermic CTCLs, the ISCL in 2002 also further established criteria and laboratory evaluation for these subtypes of CTCL.[7]

As a result of both the constantly evolving understanding of CTCL and the rarity of SS in comparison with the relatively more common CTCL variant, MF, studies have frequently grouped more indolent forms of CTCL, such as erythrodermic MF or early to later stages of MF with SS, resulting in incomplete or unstratified data on the actual survival, progression, and outcomes of documented SS.[4] Therefore, few published data exist on the long-term outcome and disease course of patients with SS. The data in the medical literature suggest a poor prognosis for this aggressive CTCL variant, with reported median overall survival ranging from 2 to 4 years.[5,7-9] When extracutaneous involvement of the viscera is identified, median survival is typically 2.5 years or less.[10-13]

At our tertiary care academic referral institution, the dermatology department evaluates and cares for a large number of patients with SS, which constitutes only about 2.5% of all CTCLs, according to data obtained from Surveillance, Epidemiology, and End Results.[14] With the incidence of CTCL increasing dramatically since the 1970s,[3] we examined the SS population at our institution over the recent decades, focusing on long-term survival and identifying prognostic factors in these patients. This collective, single-institution experience over the past 4 decades intends to supplement the literature on this more rare and aggressive lymphoma-leukemia and to compare our survival data with the literature at large.

CAPSULE SUMMARY

- Sézary syndrome is an aggressive variant of cutaneous T-cell lymphoma that is associated with a poor prognosis.
- To our knowledge, this study population is the largest of patients with Sézary syndrome reported in the medical literature and reaffirms the poor prognosis of this disease.
- This investigation analyzes prognostic factors that are specific to this group of patients and adds data to the literature on Sézary syndrome.

METHODS

The Mayo Clinic Institutional Review Board approved this study. A data retrieval specialist performed an electronic search of the medical diagnosis index to identify patients with SS diagnosed at Mayo Clinic, Rochester, MN, between 1976 and 2010. A retrospective chart review was conducted to ensure that the cases fulfilled SS diagnostic criteria. Medical records were reviewed for only the patients who had not denied access to their records for research purposes, in accordance with Minnesota Statute 144.335.

At primary evaluation, the patients generally underwent a complete physical examination, complete blood cell count, general chemistry panel, skin biopsy, and manual Sézary cell count of peripheral blood smears, or flow cytometry of peripheral blood. When lymph node or visceral involvement was suspected, patients typically underwent lymph node biopsy or fine-needle aspiration and other staging (eg, bone-marrow biopsy; additional imaging, eg, chest radiograph, computed tomography, or positron emission tomography). Given that all patients in the study had SS, data on imaging were not collected because it is not included in the 2007 ISCL/EORTC criteria (Table I).

Because the study period spanned more than 3 decades and the definition of SS evolved during this time, the diagnostic criteria in the study reflected these changes over time. For the diagnostic criteria used in this study, SS cases included those with T4 (>80% of total body surface area involved with erythroderma) and definitive leukemic involvement. In patients whose SS was diagnosed before the mid-1980s, leukemic involvement was defined as absolute Sézary cell counts greater than or equal to 1000 cells/μL, following the proposed criteria of Winkelmann.[15-17] However, beginning in the mid-1980s, clinical molecular diagnostic techniques were implemented and became incorporated into SS diagnostic criteria. Therefore, in patients who received a diagnosis of SS after the mid-1980s (and in which molecular studies were available at diagnosis), leukemic involvement consistent with SS included an absolute Sézary cell count greater than or equal to 1000 cells/μL or molecular evidence of clonality by T-cell receptor (TCR) gene rearrangement (using Southern blot or, more recently, polymerase chain reaction), or both, in the blood. In essence, SS, as defined by the 2007 ISCL/EORTC classification