RESEARCH ARTICLE
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Clinical and Prognostic Features of Erythrodermic Cutaneous T-Cell Lymphoma: A Retrospective Study of 35 Patients

Sanli H. et al.: Clinical and Prognostic Profile of Erythrodermic CTCL

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ABSTRACT
Objective: Erythrodermic cutaneous T-cell lymphomas (E-CTCL), including erythrodermic mycosis fungoides (E-MF) and Sezary syndrome (SS), are aggressive and rare CTCL variants with overlapping clinical and pathological features. Differentiating between E-MF and SS is often challenging due to non-specific symptoms and shared diagnostic criteria. This study aimed to evaluate clinical and laboratory features, progression patterns, prognostic indicators, and survival outcomes in E-CTCL patients, while comparing subgroups of E-MF, de novo SS, and secondary SS.
Material and Methods: A total of 35 patients with E-CTCL were analysed (6 E-MF, 15 de novo SS, 14 secondary SS). A comprehensive evaluation encompassed clinical and histopathological data, TNMB staging, flow cytometry findings, laboratory parameters, and survival outcomes. Statistical analyses included Kaplan-Meier survival estimates and Cox regression models.
Results: Most patients were male (74.3%) and presented with advanced-stage disease (60%). Elevated serum LDH and beta-2 microglobulin levels were common, particularly in B2 blood involvement. Female sex and eosinophilia were independent predictors of mortality. Lymph node involvement was associated with rapid progression to erythroderma. No significant survival differences were observed among E-MF, de novo SS, and secondary SS subgroups.
Conclusion: E-CTCL remains a diagnostic and therapeutic challenge. Female sex and eosinophilia emerged as key independent prognostic indicators. While survival rates did not significantly differ between E-MF and SS subgroups, the overall prognosis was poor. Larger prospective studies are needed to refine prognostic models and treatment strategies.
Keywords: erythrodermic cutaneous T-cell lymphoma, mycosis fungoides, prognosis, sezary syndrome, survival

ÖZET
Amaç: Eritrodermik mikozis fungoides (E-MF) ve Sezary sendromu'nu (SS) içeren eritrodermik kutanöz T hücreli lenfomalar (E-CTCL), agresif seyirli ve nadir görülen CTCL alt tipleri olup, örtüşen klinik ve patolojik özellikler sergiler. E-MF ile SS'yi ayırt etmek, spesifik olmayan semptomlar ve ortak tanı kriterleri nedeniyle çoğu zaman zorluk yaratmaktadır. Bu çalışma, E-CTCL hastalarında klinik ve laboratuvar özellikleri, hastalık progresyon paternlerini, prognostik göstergeleri ve sağkalım sonuçlarını değerlendirmeyi; ayrıca E-MF, de novo SS ve sekonder SS alt gruplarını karşılaştırmayı amaçlamaktadır.
Gereç ve Yöntem: Çalışmaya, E-CTCL tanısı almış toplam 35 hasta (6 E-MF, 15 de novo SS, 14 sekonder SS) dahil edildi. Klinik ve histopatolojik veriler, TNMB evrelemesi, akım sitometri bulguları, laboratuvar

parametreleri ve sağkalım sonuçlarını içeren kapsamlı bir değerlendirme yapıldı. İstatistiksel analizlerde Kaplan-Meier sağkalım eğrileri ve Cox regresyon modelleri kullanıldı.
Bulgular: Hastaların çoğu erkekti (%74,3) ve %60'ı ileri evre hastalıkla başvurdu. Serum LDH ve beta-2 mikroglobulin düzeylerinde yükseklik, özellikle B2 düzeyinde kan tutulumu olan olgularda yaygındı. Kadın cinsiyet ve eozinofili, mortalite için bağımsız risk faktörleri olarak saptandı. Lenf nodu tutulumu, eritrodermaya hızlı progresyon ile ilişkiliydi. E-MF, de novo SS ve sekonder SS alt grupları arasında sağkalım açısından anlamlı bir fark gözlenmedi.
Sonuç: E-CTCL, tanı ve tedavi açısından önemli bir klinik zorluk oluşturmaktadır. Çalışmamızda kadın cinsiyet ve eozinofili, bağımsız prognostik göstergeler olarak öne çıkmıştır. E-MF ve SS alt grupları arasında sağkalım oranları anlamlı düzeyde farklılık göstermemekle birlikte, genel prognoz kötü seyretmiştir. Prognostik modellerin geliştirilmesi ve tedavi stratejilerinin iyileştirilmesi için daha geniş kapsamlı, prospektif çalışmalara ihtiyaç vardır.
Anahtar Kelimeler: eritrodermik kutanöz T hücreli lenfoma, mikozis fungoides, prognoz, Sezary sendromu, sağkalım

INTRODUCTION

Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma (CTCL) while Sezary syndrome (SS) is an erythrodermic form with leukemic involvement. According to tumor-lymph node-metastasis-blood (TNMB) staging, erythrodermic MF (E-MF) and SS are considered aggressive CTCL variants [1, 2].

MF and SS share similar clinical, laboratory, and histological characteristics, as well as the same diagnostic approach and staging system. Whether they represent distinct entities or stages of the same disease remains debated [3]. Recent studies suggest that MF arises from clonal skin-resident $CD4^+$ effector memory T cells, while SS originates from central memory T cells expressing lymph node-homing molecules CCR7 and L-selectin [4]. E-MF presents with erythroderma and histopathological features of MF, but minimal or no SS-specific blood involvement, usually evolving from patch or plaque lesions. In contrast, SS is defined by erythroderma, lymphadenopathy, and circulating atypical lymphocytes, with erythroderma typically appearing de novo [1, 2, 5]. Due to overlapping clinical and histopathological features, assessing peripheral blood and medical history is crucial to distinguish E-MF from SS. Flow cytometry is commonly used to quantify CD4+, CD8–, CD7–, and CD26– cells [2,3], while immunohistochemistry and molecular analyses aid further differentiation.[3] Recently identified biomarkers- including PD-1, CD158k/KIR3DL2, microRNAs, MUM1, c-myb, FOXP3, T-plastin, Twist, CD335/NKp46- have shown diagnostic value in SS cases [6].

Survival in E-MF/SS is generally limited, ranging from several months to a few years. Clinical, hematological, pathological and genotypic parameters may influence survival. Male sex, older age, elevated serum lactate dehydrogenase (LDH) and beta-2 microglobulin are established poor prognostic markers [7, 8]. Folliculotropism, advanced stage, high blood tumor burden, and large cell transformation (LCT) are also linked to worse outcomes [9-11].

This single-center retrospective study aimed to evaluate the clinical and laboratory features, factors associated with progression to erythroderma, survival outcomes, and the prognostic impact of blood involvement and other variables in patients who developed erythrodermic CTCL during follow-up.

METHODS

This retrospective study included 35 patients with CTCL who developed erythroderma during the disease course, all of whom presented to the Department of Dermatology and Venereology, Ankara University Faculty of Medicine, Ankara, Türkiye between January 2005 and August 2021. The study was approved by the institutional Ethics Committee, and written informed consent was obtained from all patients.

The diagnosis of E-CTCL was based on persistent erythroderma covering at least 80% of the body surface area, with histopathological features consistent with MF/SS. Other causes of erythroderma were excluded. Patients were staged according to the TNMB staging, as outlined by the ISCL/EORTC [12]. Staging was repeated whenever disease progression occurred.

The Sezary cell count was assessed in all patients using peripheral blood smear evaluation and/or flow cytometry. Criteria for blood involvement in SS include either an absolute Sezary cell count greater than 1.000/μL or an expanded CD4+ T cell population resulting in a CD4/CD8 ratio ≥ 10, CD4+/CD7- cells ≥ 30%, or CD4+/CD26- cells ≥ 40% [13].

LCT was defined as the histological presence of large cells (four times or more the size of normal lymphocytes) comprising more than 25% of the lymphoid or tumor cell infiltration in the skin or lymph nodes.

The study evaluated patient demographics, clinicopathologic variants, TNMB staging, and laboratory parameters, including eosinophil count, serum LDH, and beta-2 microglobulin.

To enable meaningful comparisons given the relatively small sample sizes, N0–N1 were grouped as 'no lymph node involvement/dermatopathic lymphadenopathy' and N2–N3 as 'lymph node involvement'; likewise, B0–B1 were combined and compared with B2 to assess blood involvement.

Treatment modalities, disease status at last follow-up, and causes of death were recorded. Factors contributing to rapid progression to erythroderma and their impact on survival were analyzed. For survival analysis, patients were categorized into three groups: E-MF, de novo SS, and secondary SS. While de novo SS refers to patients who were erythrodermic from the outset and met the criteria for B2 blood involvement at diagnosis, secondary SS was defined as cases initially diagnosed with MF (non-leukemic) who developed erythroderma and subsequently fulfilled the criteria for B2 blood involvement during the course of follow-up.

Statistical Analysis

IBM SPSS Statistics 22 software was used for statistical analyses in this study. The normality of the parameters was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Descriptive statistical methods were employed to summarise the data, including the minimum, maximum, mean, standard deviation, median, interquartile range, and frequency. In order to compare quantitative data, the Kruskal-Wallis test was used for non-normally distributed parameters among groups, while the Mann-Whitney U test was used for comparisons between two groups.

The Fisher's Exact Chi-Square test was applied for the comparison of categorical data. Spearman's rho correlation analysis was utilized to examine relationships between parameters that did not follow a normal distribution.

Survival analysis was performed using the Kaplan-Meier method, and survival probabilities were compared using the log-rank test. Cox regression analysis was conducted as a multivariate analysis. The statistical significance level was accepted as $p < 0.05$.

RESULTS

From a database of 342 CTCL patients, a total of 35 erythrodermic patients (6 E-MF, 15 de novo SS and 14 secondary SS) were selected for further analysis. The median follow-up period was 52.6 months. The study included 26 males (74.3%) and 9 females (25.7%). The mean age at diagnosis was 54.09 ± 14.64 years. The most prevalent clinicopathologic variant was folliculotropic MF, followed by classic, poikilodermatous and ichthyosiform MF.

Of the 35 patients, 5 (14.3%) were stage IB, 9 (25.7%) stage IIA, 1 (2.9%) stage IIB, 5 (14.3%) stage IIIA, and 15 (42.8%) stage IVA at diagnosis. Overall, 14 patients (40%) were in early stages and 21 (60%) in advanced stages. At the last visit, 5 (14.3%) were stage IIIA, 1 (2.9%) stage IIIB, and 28 (82.9%) stage IVA.

MF lesions preceding erythroderma were seen in 20 patients (57.1%), including all E-MF cases and 14 with secondary SS. The remaining 15 patients (42.9%) presented with de novo erythroderma, all of whom were diagnosed with SS.

Histopathological evaluation showed lymph node involvement in 20 patients (57.1%), with classifications as follows: N0 in 1 patient (2.9%), N1 in 10 (28.6%), N2 in 12 (34.3%), and N3 in 8 (22.9%). In four patients, radiological findings indicated pathological lymph nodes, but histopathological examination could not be performed due to refusal of biopsy (Nx).

Of the 35 patients, 29 (82.9%) were B2, 1 (2.9%) B1, and 5 (14.3%) B0. All de novo SS cases were B2 at diagnosis, while 14 secondary SS patients developed blood involvement during follow-up. Flow cytometry revealed a median CD4/CD8 ratio of 5.4, with median percentages of CD4+CD7− and CD4+CD26− lymphocytes being 38% and 58.5%, respectively.

The median serum eosinophil count was 0.8×10^9/L (range: 0.11–13.02), the median LDH level was 517 U/L (range: 234–2095), and the median beta-2 microglobulin level was 4.89 mg/L (range: 2.63–12.8).

Serum LDH levels (normal range: 135–214 U/L) were elevated in all patients, while beta-2 microglobulin levels (normal range: 1.09–2.53 mg/L) were elevated in 32 patients (91.4%), and eosinophilia (serum eosinophil count $>0.7 \times 10^9$/L) was observed in 20 patients (57.1%).

Ten out of the 35 patients (28.6%) exhibited LCT in skin or lymph node biopsies. Tumoral lesions accompanied erythroderma in only one patient (2.85%).

Patients received a variety of treatments, including extracorporeal photopheresis (ECP), phototherapy, interferon, acitretin, oral bexarotene, methotrexate, brentuximab vedotin, and other chemotherapies.

Most patients (94.2%) were treated with combination therapies, with ECP being the most commonly used (74.3%), followed by phototherapy (62.9%) and interferon (60%). Allogeneic stem cell transplantation was performed in eight patients—five with de novo SS, two with secondary SS, and one with E-MF. Complete remission was achieved in three patients (two with de novo SS and one with secondary SS), with a mean relapse-free follow-up of 107 months (range: 76–132).

At the last follow-up, 25 patients (71.4%) had died, with lymphoma being the primary cause in 68% of cases. Infections and other causes each accounted for 16% of the deaths. Demographic and clinical characteristics of the patients are summarized in Table 1.

The mean serum eosinophil count, LDH, and beta-2 microglobulin levels were higher in patients with B2-stage blood involvement compared to those with B0 and B1 stages; however, these differences were not statistically significant ($p > 0.05$).

In the evaluation of factors influencing the time from initial symptoms to the development of erythroderma, sex, clinicopathological variants, presence of LCT, and disease stage at diagnosis were not found to be significant. However, patients with advanced lymph node involvement (N2/N3) showed a significantly faster progression to erythroderma ($p = 0.042$). Additionally, a moderately strong inverse correlation was observed between serum LDH levels and the time from symptom onset to erythroderma ($r = –0.428$, $p = 0.01$). No significant correlations were found between this duration and serum eosinophil count or beta-2 microglobulin levels ($p > 0.05$).

The duration from the onset of erythroderma to death was significantly shorter in female patients compared to males (5.5 months vs. 39 months, $p = 0.007$). No significant correlations were observed with other variables, including laboratory parameters ($p > 0.05$).

Although deceased patients exhibited higher CD4/CD8 ratios and increased percentages of $CD4^+CD7^–$ and $CD4^+CD26^–$ lymphocytes compared to survivors, these differences were not statistically significant ($p > 0.05$).

At the last follow-up, mortality rates were 80% in de novo SS (12/15), 64.3% in secondary SS (9/14), and 66.7% in E-MF (4/6), with no significant difference between groups ($p = 0.611$) (Table 2).

In the de novo SS group, the last death occurred at month 121, with a cumulative survival of 8.2%. The mean survival time was 57.21 ± 11.32 months (median: 51 months), and the 5-year survival rate was 41%. In the secondary SS group, the last death occurred at month 92, with a cumulative survival of 15.3%. The mean survival time was 47.84 ± 12.14 months (median: 24 months), and the 5-year survival rate was 30.6%. In the E-MF group, the last death occurred at month 62, with a cumulative survival rate of 0.0%. The mean survival time was 44.04 ± 8.44 months (median: 48 months), and the 5-year survival rate was 0% (Table 3, Figure 1).

Univariate and multivariate Cox regression analyses identified female sex as an independent risk factor for mortality. In the univariate model, females had a 3.32-fold higher risk of death (HR: 3.32, 95% CI: 1.20–9.22, $p = 0.021$), which increased to 17.47-fold in the multivariate model (HR: 17.47, 95% CI: 2.33–130.94, $p = 0.005$). While eosinophilia was not significant in univariate analysis ($p = 0.229$), it became a significant predictor in the multivariate model (HR: 1.76, 95% CI: 1.08–2.86, $p = 0.024$).

Other variables—including age >60, B2 blood involvement, advanced stage, LCT, N2/N3 lymph node involvement, folliculotropism, LDH levels, beta-2 microglobulin levels, CD4/CD8 ratio, and CD7 or CD26 loss—were not significantly associated with mortality in either model ($p > 0.05$) (Table 4).

DISCUSSION

The prognostic factors in E-CTCL remain poorly defined due to the rarity of the disease and inherent diagnostic complexities. In this study, we evaluated 35 patients with E-CTCL (10.2%) out of a total of 342 CTCL cases. This proportion of erythrodermic cases is consistent with the mean prevalence of 10% reported in previous studies [(2)].

In the existing literature, the mean age of patients with MF is reported to be between the fifth and sixth decades, with a male-to-female incidence ratio ranging from 1.6:1 to 1.9:1 [(14-16)]. In our cohort, the mean age at diagnosis was 54.09 years, consistent with previous findings. However, the male-to-female ratio was notably higher, and this elevated ratio may be explained by the tendency for males to be diagnosed at more advanced T stages compared to females[(17)], consistent with the predominance of advanced-stage cases in our study.

Advanced age at diagnosis has been identified as an independent adverse prognostic factor in several studies [(8, 18-20)]. However, in our cohort of patients with E-CTCL, age did not emerge as a significant predictor of mortality.

The prognostic impact of sex also remains a subject of debate. While some studies, have reported worse outcomes in male patients irrespective of disease stage[(18, 19)], this finding has not been consistently replicated. Schmid et al. reported significantly better survival rates among males with CTCL compared to their female counterparts [(21)]. Furthermore, a study by Lim et al., which included 246 patients with MF/SS, demonstrated that male patients had a significantly longer mean recurrence-free survival compared to female patients ($p = 0.008$) [(22)]. In our study, female sex emerged as a significant risk factor for mortality.

Folliculotropic MF (FMF) is the most frequent clinicopathologic variant of MF. A prior single-center study from our institution involving 53 FMF patients reported advanced-stage disease in 45.3% at diagnosis and disease progression in 52.3% during follow-up [(23)]. Its relatively high prevalence in our cohort may reflect both the established predominance of FMF and the referral-based nature of our center. However, despite this, our study did not identify folliculotropism as a significant prognostic indicator in E-CTCL patients.

Elevated levels of LDH, beta-2 microglobulin and serum eosinophil count have previously been associated with advanced stages of MF/SS [(2, 8, 19, 24-26)]. Elevated serum LDH is a well-established poor prognostic marker in both solid tumors and hematologic malignancies, reflecting tumor burden and invasiveness [(27)]. In a study by Al Saif et al., elevated LDH was observed in 20% of stage IB, 50% of stage IIA, and 100% of advanced-stage MF cases [(24)]. Similarly, all patients in our cohort had elevated LDH. Notably, those with higher LDH levels developed erythroderma more rapidly after symptom onset.

Elevated beta-2 microglobulin levels have been linked to shorter survival and higher risk of progression in MF [(7, 8)]. In our study, levels increased with advancing B stage, but the trend was not statistically significant.

As in other T-cell malignancies and Hodgkin lymphoma, eosinophilia is common in CTCL, likely due to Th2 cytokine overproduction by malignant T cells. Since Th1 responses are essential for antitumor immunity, a Th2-

dominant profile may impair tumor control and increase infection risk, making eosinophilia a potential marker of poor prognosis. In a study involving 104 CTCL patients, eosinophilia was the only independent predictor of disease progression and disease-specific mortality [25]. Similarly, we found higher mortality in patients with eosinophilia. While prior studies reported eosinophilia in ~20% of CTCL cases, it was more frequent in our cohort (57.1%), likely due to a higher proportion of advanced-stage erythrodermic patients.

In our cohort, patients with advanced lymph node involvement (N2/N3) progressed to erythroderma more rapidly than those without. Agar et al. reported poorer survival in patients with dermatopathic lymphadenopathy, with N2-stage nodes showing a similar mortality risk as N3-stage [19]. However, we found no significant difference in mortality between patients with and without advanced nodal involvement.

In a study by the Cutaneous Lymphoma International Consortium (CLIC) involving 1,275 patients with advanced MF/SS, the median overall survival was 63 months, with a 5-year survival rate of 52%. Stage IV, age >60 years, LCT, and elevated LDH were identified as independent prognostic markers for poorer survival [28].

We did not identify LCT, folliculotropism, or flow cytometry parameters as significant prognostic indicators in E-CTCL patients. This discrepancy may be due to the relatively small sample size of our cohort, which could limit the statistical power to detect such associations. Notably, unlike the CLIC study, our cohort exclusively comprised individuals who were clinically erythrodermic at the time of inclusion, enabling a focused assessment of this distinct clinical phenotype. A key contribution of our study is the stratification of erythrodermic patients into three clinically relevant subgroups offering a novel framework to investigate prognostic variability within E-CTCL. Furthermore, our inclusion of patients who progressed from non-erythrodermic stages to erythroderma provides valuable insight into the natural history and evolution of CTCL, offering a complementary perspective to existing large-scale datasets.

The classification of E-CTCL remains complex, with considerable clinical and biological overlap between entities. Recent reports have highlighted that a subset of patients with SS may present without erythroderma, despite fulfilling hematologic criteria (B2 blood involvement) [29]. In some of these cases, erythroderma may never develop during the disease course, suggesting that SS may span a broader clinical spectrum than previously recognized.

Adding to this complexity, there is ongoing debate regarding the appropriate terminology for patients initially diagnosed with MF who later develop B2 blood involvement. While some authors classify these cases as SS, others favor designations such as secondary SS or SS preceded by MF [30]. In our study, we adopted the term secondary SS for such cases.

We initially hypothesized that de novo SS cases would demonstrate poorer survival compared to other subgroups. However, our findings did not support this assumption, indicating no statistically significant survival difference between de novo SS, secondary SS, and E-MF groups. This may be partly explained by limitations inherent to our study design, including the relatively small sample size, its retrospective nature, and the lack of molecular diagnostic tools to better delineate overlapping clinical entities. Alternatively, the findings suggest that prognostic stratification in E-CTCL may not solely depend on the timing or sequence of erythroderma and hematologic involvement, underscoring the need for more refined biological markers to accurately predict disease trajectory.

CONCLUSION

These findings underscore the aggressive nature and limited survival outcomes associated with E-CTCL, regardless of subtype. Although female sex and eosinophilia were independent predictors of mortality, and N2/N3 lymph node involvement and elevated LDH levels were linked to more rapid progression to erythroderma, no single factor definitively stratified prognosis. Prospective, large-scale studies integrating molecular diagnostics are essential to improve prognostic accuracy and inform treatment strategies in this complex patient population.

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The patients in this manuscript have given written informed consent to publication of their case details.

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All authors read and approved the final manuscript.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

REFERENCES

1. Kamijo H, Sugaya M. Two distinct variants of mycosis fungoides (MF): Folliculotropic MF and erythrodermic MF. J Dermatol. 2019;46(12):1136-40.
2. Vidulich KA, Talpur R, Bassett RL, Duvic M. Overall survival in erythrodermic cutaneous T-cell lymphoma: an analysis of prognostic factors in a cohort of patients with erythrodermic cutaneous T-cell lymphoma. Int J Dermatol. 2009;48(3):243-52.
3. Rittig AH, Lindahl LM, Johansen C, Celis P, Ødum N, Iversen L, et al. The MicroRNA Expression Profile Differs Between Erythrodermic Mycosis Fungoides and Sézary Syndrome. Acta Derm Venereol. 2019;99(12):1148-53.
4. Campbell JJ, Clark RA, Watanabe R, Kupper TS. Sezary syndrome and mycosis fungoides arise from distinct T-cell subsets: a biologic rationale for their distinct clinical behaviors. Blood. 2010;116(5):767-71.
5. Vonderheid EC, Bernengo MG, Burg G, Duvic M, Heald P, Laroche L, et al. Update on erythrodermic cutaneous T-cell lymphoma: report of the International Society for Cutaneous Lymphomas. J Am Acad Dermatol. 2002;46(1):95-106.
6. Hurabielle C, Michel L, Ram-Wolff C, Battistella M, Jean-Louis F, Beylot-Barry M, et al. Expression of Sézary Biomarkers in the Blood of Patients with Erythrodermic Mycosis Fungoides. J Invest Dermatol. 2016;136(1):317-20.
7. Diamandidou E, Colome M, Fayad L, Duvic M, Kurzrock R. Prognostic factor analysis in mycosis fungoides/Sézary syndrome. J Am Acad Dermatol. 1999;40(6 Pt 1):914-24.
8. Talpur R, Singh L, Daulat S, Liu P, Seyfer S, Trynosky T, et al. Long-term outcomes of 1,263 patients with mycosis fungoides and Sézary syndrome from 1982 to 2009. Clin Cancer Res. 2012;18(18):5051-60.
9. Scarisbrick JJ, Kim YH, Whittaker SJ, Wood GS, Vermeer MH, Prince HM, et al. Prognostic factors, prognostic indices and staging in mycosis fungoides and Sézary syndrome: where are we now? Br J Dermatol. 2014;170(6):1226-36.
10. Miyagaki T, Sugaya M. Erythrodermic cutaneous T-cell lymphoma: how to differentiate this rare disease from atopic dermatitis. J Dermatol Sci. 2011;64(1):1-6.
11. Skayem C, Beylot-Barry M, de Masson A, Dereure O, Ram-Wolff C, Bagot M, et al. Lymph node and visceral progression without erythroderma or blood worsening in erythrodermic cutaneous T-cell lymphoma: nine cases. Br J Dermatol. 2021;185(5):1061-3.
12. Olsen E, Vonderheid E, Pimpinelli N, Willemze R, Kim Y, Knobler R, et al. Revisions to the staging and classification of mycosis fungoides and Sezary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer (EORTC). Blood. 2007;110(6):1713-22.
13. Willemze R, Cerroni L, Kempf W, Berti E, Facchetti F, Swerdlow SH, et al. The 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas. Blood. 2019;133(16):1703-14.
14. Quaglino P, Pimpinelli N, Berti E, Calzavara-Pinton P, Alfonso Lombardo G, Rupoli S, et al. Time course, clinical pathways, and long-term hazards risk trends of disease progression in patients with classic mycosis fungoides: a multicenter, retrospective follow-up study from the Italian Group of Cutaneous Lymphomas. Cancer. 2012;118(23):5830-9.
15. Bradford PT, Devesa SS, Anderson WF, Toro JR. Cutaneous lymphoma incidence patterns in the United States: a population-based study of 3884 cases. Blood. 2009;113(21):5064-73.
16. Martinez XU, Di Raimondo C, Abdulla FR, Zain J, Rosen ST, Querfeld C. Leukaemic variants of cutaneous T-cell lymphoma: Erythrodermic mycosis fungoides and Sézary syndrome. Best Pract Res Clin Haematol. 2019;32(3):239-52.
17. Wilson LD, Hinds GA, Yu JB. Age, race, sex, stage, and incidence of cutaneous lymphoma. Clin Lymphoma Myeloma Leuk. 2012;12(5):291-6.
18. Benton EC, Crichton S, Talpur R, Agar NS, Fields PA, Wedgeworth E, et al. A cutaneous lymphoma international prognostic index (CLIPi) for mycosis fungoides and Sezary syndrome. Eur J Cancer. 2013;49(13):2859-68.
19. Agar NS, Wedgeworth E, Crichton S, Mitchell TJ, Cox M, Ferreira S, et al. Survival outcomes and prognostic factors in mycosis fungoides/Sézary syndrome: validation of the revised International Society for Cutaneous Lymphomas/European Organisation for Research and Treatment of Cancer staging proposal. J Clin Oncol. 2010;28(31):4730-9.
20. Suzuki SY, Ito K, Ito M, Kawai K. Prognosis of 100 Japanese patients with mycosis fungoides and Sézary syndrome. J Dermatol Sci. 2010;57(1):37-43.

21. Schmid MH, Bird P, Dummer R, Kempf W, Burg G. Tumor burden index as a prognostic tool for cutaneous T-cell lymphoma: a new concept. Arch Dermatol. 1999;135(10):1204-8.
22. Lim HLJ, Tan EST, Tee SI, Ho ZY, Boey JJJ, Tan WP, et al. Epidemiology and prognostic factors for mycosis fungoides and Sézary syndrome in a multi-ethnic Asian cohort: a 12-year review. J Eur Acad Dermatol Venereol. 2019;33(8):1513-21.
23. Kalay Yildizhan I, Sanli H, Akay BN, Uzundere C, Okcu Heper A. Folliculotropic mycosis fungoides: Clinical characteristics, treatments, and long-term outcomes of 53 patients in a tertiary hospital. Dermatol Ther. 2020;33(4):e13585.
24. Saif F. Prognostic Significance of Serum Lactate Dehydrogenase in Saudi Patients with Mycosis Fungoides: A Retrospective Study of 47 Patients. Journal of Clinical & Experimental Dermatology Research. 2016;07.
25. Tancrède-Bohin E, Ionescu MA, de La Salmonière P, Dupuy A, Rivet J, Rybojad M, et al. Prognostic value of blood eosinophilia in primary cutaneous T-cell lymphomas. Arch Dermatol. 2004;140(9):1057-61.
26. Bahalı AG, Su O, Cengiz FP, Emiroğlu N, Ozkaya DB, Onsun N. Prognostic factors of patients with mycosis fungoides. Postepy Dermatol Alergol. 2020;37(5):796-9.
27. Walenta S, Mueller-Klieser WF. Lactate: mirror and motor of tumor malignancy. Semin Radiat Oncol. 2004;14(3):267-74.
28. Scarisbrick JJ, Prince HM, Vermeer MH, Quaglino P, Horwitz S, Porcu P, et al. Cutaneous Lymphoma International Consortium Study of Outcome in Advanced Stages of Mycosis Fungoides and Sézary Syndrome: Effect of Specific Prognostic Markers on Survival and Development of a Prognostic Model. J Clin Oncol. 2015;33(32):3766-73.
29. Kamijo H, Miyagaki T, Norimatsu Y, Shishido-Takahashi N, Kuzumi A, Asano Y, et al. Sézary syndrome without erythroderma: A case report and review of published work. J Dermatol. 2019;46(1):61-4.
30. Cetinözman F, Jansen PM, Vermeer MH, Willemze R. Differential expression of programmed death-1 (PD-1) in Sézary syndrome and mycosis fungoides. Arch Dermatol. 2012;148(12):1379-85.

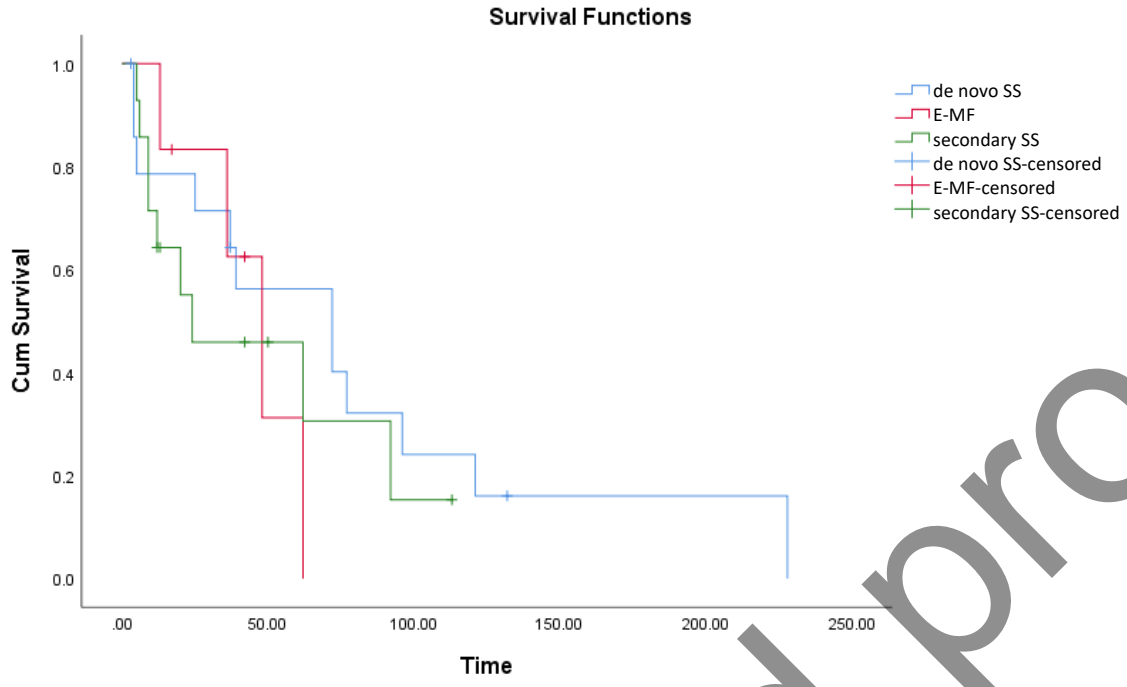

Figure 1: Kaplan–Meier survival curves for patients with de novo SS, secondary SS, and E-MF ($p > 0.05$).

Table 1: Demographic and clinical characteristics of the patients with E-CTCL.

	Value
Current age Mean±SD (Min-Max)	62.31±12.97 (39-83)
Age at diagnosis Mean±SD (Min-Max)	54.09±14.64 (23-76)
Gender n (%)	
Male	26 (74.3%)
Female	9 (25.7%)
MF variants * n (%)	
Folliculotropic	14 (40%)
Classic	13 (37.1%)
Poikilodermatous	6 (17.1%)
Ichthyosiform	2 (5.7%)
Clinical stage at diagnosis n (%)	
IB	5 (14.3%)
IIA	9 (25.7%)
IIB	1 (2.9%)
IIIA	5 (14.3%)
IVA	15 (42.8%)
Clinical stage at last visit n (%)	
IIIA	5 (14.3%)
IIIB	1 (2.9%)
IVA	29 (82.9%)
De novo erythroderma n (%)	
Yes	15 (42.9%)
No	20 (57.1%)
Lymph node involvement n (%)	
N0	1 (2.9%)
N1	10 (28.6%)
N2	12 (34.3%)
N3	8 (22.9%)

Nx	4 (11.4%)
Blood involvement n (%)	
B0	5 (14.3%)
B1	1 (2.9%)
B2	29 (82.9%)
Treatment modalities n (%)	
ECP	26 (74.3%)
Interferon	21 (60%)
Phototherapy	22 (62.9%)
Acitretin	10 (28.6%)
Oral bexarotene	2 (5.7%)
Methotrexate	5 (14.3%)
Brentuximab	8 (22.8%)
Other chemotherapies	16 (45.7%)
AHSCT	8 (22.8%)
Status at last follow-up n (%)	
Dead	25 (71.4%)
Alive	10 (28.6%)
Cause of death n (%)	
Lymphoma-related	17 (68%)
Infectious	4 (16%)
Other	4 (16%)

AHSCT, allogeneic hematopoietic stem cell transplantation; ECP, extracorporeal photopheresis; MF, mycosis fungoides; Min: minimum; Max: maximum; N: number; SD: standard deviation.
*: Table includes all MF clinicopathologic variants that were observed with erythroderma during the disease course.

Table 2: Mortality rates according to the diagnosis

	Mortality		
	Dead	**Alive**	
Diagnosis	**n (%)**	**n (%)**	**p**
De novo SS	12 (80.0)	3 (20.0)	0.611
Secondary SS	9 (64.3)	5 (35.7)	
E-MF	4 (66.7)	2 (33.3)	

Fisher's Exact test
E-MF, erythrodermic mycosis fungoides; N: number; SS, sezary syndrome.

Table 3: Survival outcomes in patients with de novo SS, secondary SS, and E-MF.

	Number of patients	**Latest time of death**	**Cumulative Survival**	**Std. Error**	**OS**			
					Median	**Lower CI**	**Upper CI**	**Mean±SE**
DE NOVO SS	15	121	0.082	19.103	51	13.558	88.442	57.21 ± 11.32
SECONDARY SS	14	92	0.153	24.504	24	0.000	72.029	47.84 ± 12.14
E-MF	6	62	0.000	9.423	48	29.530	66.470	44.04 ± 8.44
OVERALL	35			11.452	48	25.554	70.446	52.24 ± 7.49

CI, confidence interval; MF, mycosis fungoides; SE, standart error; SS, sezary syndrome; OS, overall survival.

Table 4: Univariate and multivariate Cox regression analyses for factors associated with mortality in E-CTCL.

	Univariate			Multivariate		
	HR	95% CI	p	HR	95% CI	p
Age (>60 years)	0.95	(0.35-1.81)	0.585	0.60	(0.03-10.61)	0.729
Sex (Female)	3.21	(1.20-9.22)	**0.021***	17.47	(2.33-130.94)	**0.005***
Blood involvement (B2)	1.07	(0.33-2.66)	0.908	0.90	(0.04-18.41)	0.946
LCT (Yes)	1.17	(0.32-2.06)	0.664	0.08	(0.01-1.36)	0.081
Advanced stage at diagnosis	0.61	(0.22-1.21)	0.127	0.00	(0.00-1.53)	0.066
LN involvement (N2-N3)	0.46	(0.14-1.16)	0.091	0.39	(0.02-6.82)	0.520
Folliculotropism	1.37	(0.69-3.88)	0.262	0.09	(0.00-3.82)	0.205
Eosinophilia	0.92	(0.84-1.04)	0.229	1.76	(1.08-2.86)	**0.024***
LDH	1.00	(1.00-1.00)	0.812	1.00	(1.00-1.01)	0.322
Beta-2 microglobulin	0.85	(0.75-1.08)	0.255	1.20	(0.72-2.00)	0.483
CD4/CD8	1.01	(0.99-1.02)	0.558	1.02	(0.97-1.06)	0.455
CD7-	0.99	(0.98-1.01)	0.386	0.97	(0.93-1.00)	0.056
CD26-	1.01	(0.98-1.02)	0.938	1.09	(0.99-1.20)	0.070

CI, confidence interval; HR, hazard ratio; LCT: large cell transformation; LDH, lactate dehydrogenase; LN: lymph node