Introduction

Cutaneous T-cell lymphomas (CTCL) are a heterogeneous group of non-Hodgkin lymphomas characterized by skin-homing neoplastic T cells. Mycosis fungoides (MF) is the most common form of CTCL (54–72%). The overall annual age-adjusted incidence of CTCL is 6.4 × 10−6. Incidence rate is higher among African Americans compared to Caucasians (9.0 × 10−6 vs 6.1 × 10−6) and higher among males compared to females (8.7 × 10−6 vs 4.6 × 10−6) (2). Median age at diagnosis is 55–60 years. Stage of MF is based on skin (T), lymph node (N), visceral (M), and blood (B) involvement (TNMB). Of these stages, T stage and the presence of extracutaneous disease are the most important factors for survival. Early-stage disease (IA-IIA) portends a good prognosis compared to advanced stage disease (IIB-IVB). The overall annual age-adjusted predicted 10-year overall survival (OS) rates are 90.3% and 53.2% for early and advanced stage disease, respectively. Early-stage disease (IA–IIA) presents with scaly patches alone (T1a/T2a) or patches and plaques T1b/T2b) of different shapes and sizes, mostly located on the sun-protected areas of the body. Early-stage disease mimics a variety of skin conditions, with mean delay of 36 months from the time of onset to the final diagnosis. Up to one third of patients with early-stage disease may progress to advanced disease. Advanced stage disease presents with widespread patches or plaques with internal organ and/or blood involvement. Three percent of patients with MF progress to Sezary syndrome (SS). SS is a leukemic form of CTCL, which presents with erythroderma, generalized adenopathy, and peripheral blood involvement. Prognostic factors in MF are less well-defined compared to other lymphomas due to lack of large cohorts, disease rarity, and diagnostic challenges.

Materials and Methods

We conducted a literature review of PubMed in November 2021 to identify prognostic factors in MF. We reviewed the medical literature (PubMed and Ovid Medline databases) in August 2021, using Mesh key terms ‘prognostic factor’, ‘prognostic indicator’, ‘mycosis fungoides’, ‘Sezary syndrome’, ‘Skin Lymphoma’, ‘Cutaneous Lymphoma’ to identify the case reports, case series, studies and review articles about MF. Further papers were also identified from the reference lists of the above retrieved papers and citations. Our search included articles in the English-language, published between 1981 and 2020. The selection process included first the screening of titles and abstracts and then the evaluation of the full text articles. We included data from publicly available online reports and this review did not qualify as human subject research; therefore, institutional review board approval was not required at the Saint Peter’s University Hospital.

Results

Mycosis fungoides have broad range of clinical presentation and outcomes. MF commonly presents in older individuals with a peak incidence be-tween the 6th–7th decades of life but can begin as early as 1st decade. Prognosis of the disease strongly depends on the age at diagnosis. Older age is associated with poorer prognosis. MF incidence and disease course differs based on sex. Males have a higher incidence and have worse prognosis than females regardless of disease stage. The strongest prognostic factor in MF patients is the stage of the disease which consists of extension of disease (skin, blood, distant organs), tumourality and involvement of lymph nodes. The presence in blood of T-cell clones (identical to skin clones) in Flow cytometry is a qualitative diagnostic criterion for MF. Search for circulating Sezary cells is essential to determine the stage and the prognosis. To diagnose B2 stage which associated with poor prognosis, T-cell receptor clonal rearrangement in blood as well as one of the follow-ing criteria is required: Sezary cell count >1000/mm3, CD4/CD8 > 10, loss of CD7 expression >40% or CD 26 expression >30%. Another emerging peripheral blood marker for prognosis is KIR3DL1. Lactate dehydrogenase (LDH) is a non-specific marker of tumor burden and has been associated with poor prognosis in advanced stage. Eosinophilia has been attributed to TH2 predominance leading to interleukin-5 (an eosinophilic cytokine) expression by neoplastic T cells. But in MF, TH1 cells play a key role for initiation and maintenance of anti-tumor response against neoplastic T cells. TH2 pre-dominance is associated with reduced antitumoral response in MF lesions. A few studies showed a decreased survival and increased disease progression rate in cases of MF with eosinophilia. Large cell transformation (LCT) is defined by the presence of CD30– or CD30+ large cells (at least 4 times larger than a small lymphocyte) exceeding 25% of the infiltrate or forming microscopic nodules. Early LCT occurring <2 years from diagnosis as well as LCT occurring at advanced stage disease is associated with poor prognosis.

Conclusion

The strongest prognostic factor in MF patients is the stage of the disease. T stage and the presence of extracutaneous disease are the most important factors for survival. Other factors that are associated with worse prognosis are male gender, advanced age, presence of plaques and tumors, folliculotropism and lymph node stage above N1/Nx. Mycosis fungoides is a rare disease with poorly understood biology and a broad range of clinical presentation and outcomes. Because longitudinal data are scarce, prognostic indicators are ill-defined. Thus, there is a need for validated prognostic tools to assess disease progression risk among heterogeneous groups of MF patients. The findings presented here illustrated that disease prognosis in early stages depends on many contributing factors. Detection and stratification of these factors may allow personalized approach to management of these patients. There is a tremendous effort underway to validate these and other factors to stratify patients into risk groups in the near future.

References