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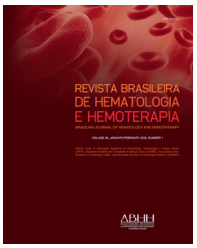

Original article

High frequency of primary refractory disease and low progression-free survival rate of Hodgkin's lymphoma: a decade of experience in a Latin American center

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ABSTRACT

Background: Reports dealing with clinical outcomes of classical Hodgkin's lymphoma in low- to middle-income countries are scarce and response to therapy is poorly documented. This report describes the characteristics and clinical outcomes of patients with classical Hodgkin's lymphoma from a single institution in Latin America.

Method: A retrospective study was conducted over ten years of patients with classical Hodgkin's lymphoma treated at a referral center. Progression-free and overall survival rates were estimated by Kaplan–Meier analysis. The univariate Cox regression model was used to estimate associations between important variables and clinical outcomes.

Main results: One hundred and twenty-eight patients were analyzed. The mean age was 28.5 years. The five-year progression-free and overall survival were 37.3% and 78.9%, respectively. Of the whole group, 55 (43%) were primary refractory cases. Only 39/83 (47%) patients with advanced disease vs. 34/45 (75.6%) in early stages (p-value = 0.002) achieved complete remission. Those with advanced disease had a five-year overall survival of 68.7% vs. 91.8% for early disease (p-value = 0.132). Thirty-one patients relapsed (24.2%) and 20 (64.5%) received a transplant. The hazard ratio for progression with bone marrow infiltration was 2.628 (p-value = 0.037). For death, an International Prognostic Score $\geq$4 had a hazard ratio of 3.355 (p-value = 0.050) in univariate analysis. Two-thirds of classical Hodgkin's lymphoma patients diagnosed at advanced stages had a low progression-free survival but an overall survival similar to high-income countries.

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Conclusion: Patients belonging to the general population diagnosed with classical Hodgkin's lymphoma in Northeastern Mexico had a significantly low progression-free survival rate and presented with advanced disease, underscoring the need for earlier diagnosis and improved contemporary therapeutic strategies in these mainly young productive-age Hodgkin's lymphoma patients.

Introduction

Hodgkin's lymphoma (HL) is one of the most common malignancies in the young population; it has a bimodal distribution, first between 15 and 34 years of age and then after 55 years.[1] This hematologic neoplasm affects approximately 9050 new patients in the United States each year and 5000 in Latin America,[2] thus a low incidence but with high mortality is observed in Mexico.[3] Furthermore, a lower overall survival (OS) has been observed in Hispanics living in the United States, with the diagnosis established at more advanced stages and with a greater male prevalence.[4,5]

Contrary to non-Hodgkin lymphoma, the incidence of HL has remained constant over time.[1] Two distinct disease entities compose HL, classical (cHL) and the rare nodular lymphocyte predominant HL, which comprises only 5% of all cases.[6] Although HL is highly responsive to chemotherapy, approximately one third of patients with an advanced stage will have primary resistant disease[7] or will relapse after conventional treatment.[8] Standard treatment in these cases is based on autologous hematopoietic stem cell transplantation (HSCT) or high doses of chemotherapy, with the PFS reaching 30–50% in patients with relapsed disease and 20–40% in patients with refractory HL.[9–11]

There is scarce information on the characteristics of HL patients in populations where most individuals are diagnosed in advanced stages. This study reports a comprehensive descriptive analysis of incidence patterns, clinical evolution, and treatment outcomes of low-income uninsured patients with HL attending a public referral center for the general population in Northeastern Mexico over a ten-year period.

Methods

This observational, longitudinal and retrospective study included patients with a diagnosis of HL treated at the Hematology Department of the Dr. José E. González University Hospital of the School of Medicine, Universidad Autónoma de Nuevo León in Monterrey, Mexico between January 2005 and September 2015. Clinical and electronic records as well as histopathology records were reviewed and frequencies for each subtype of lymphoma were determined. The study protocol was approved by the Research Ethics Committee of the institution.

Clinical data including age, gender, Ann Arbor stage, presence or absence of B-symptoms, initial complete blood count (CBC), International Prognostic Score (IPS), bulky disease, treatment regimen and survival data were accrued and analyzed. Advanced disease was defined as bulky disease or an Ann Arbor stage III–IV. Two groups were defined according to the IPS: low risk (score: 0–3) and high risk (score: 4–7). To define HL subtypes, cases were reviewed by a hematopathologist with the immunohistochemical profile of HL being investigated in 83% of the studied patients including the following biomarkers: CD30, CD15, CD20, CD3, CD45, ALK-1, and PAX-5.[12] Due to financial restrictions at this public institution caring for patients without health insurance coverage, the Epstein–Barr virus (EBV) status was not documented in the biopsies. A computed tomography (CT) scan was performed in all patients for stratification and was reviewed by radiologists with expertise in staging lymphomas. Only selected patients were submitted to a bone marrow (BM) biopsy – patients with an Ann Arbor stage ≥III or with B-symptoms had an indication for this procedure. In this respect, it has previously been shown that only about 2% of patients in this population with HL have a positive BM biopsy.[13]

Treatment

Patients received a chemotherapy regimen chosen by the treating physician according to standard protocols including ABVD (adriamycin, bleomycin, vincristine and dacarbazine) or COPP/ABV (cyclophosphamide, vincristine, prednisone, procarbazine, doxorubicin, bleomycin and vinblastine).[14] All drugs were from original manufacturers with no generic brands administered. Some patients with bulky disease received complementary radiotherapy (RT), using intensity-modulated radiotherapy (IMRT) at doses of 30–36 Gy depending on the tumor size. The protocol consists of the delivery of 1.5–2 Gy per day until completion.[15] However, not all of these patients were treated at the study center and radiotherapy is not a regular part of the standard protocol; this is intended to limit radio-toxicity in patients customarily presenting with advanced disease. Autologous HSCT, based on a reduced intensity conditioning regimen,[16] was carried out in patients with a poor prognosis, including those who relapsed in <12 months, those who relapsed at previously irradiated sites, had disease regression <50% after 4–6 cycles of chemotherapy, or disease progression during induction or within 90 days after the end of first-line treatment.

Follow-up

Positron emission tomography (PET) studies were not available during the study period and thus classification of HL

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