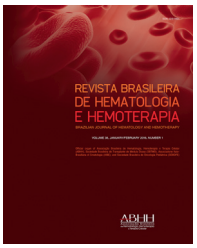
REV BRAS HEMATOL HEMOTER. 2016;xxx(xx):xxx–xxx

Revista Brasileira de Hematologia e Hemoterapia
Brazilian Journal of Hematology and Hemotherapy

www.rbhh.org



Original article

Adult T-cell leukemia/lymphoma treatment in Bahia, Brazil

Pedro Dantas Oliveira[a,*], *Ítala Gomes*[a], *Victor Hugo Gomes Souza*[b], *Ernesto Cunha Pires*[c], *Glória Bomfim Arruda*[a], *Achiléa Bittencourt*[a]

[a] *Universidade Federal da Bahia (UFBA), Salvador, BA, Brazil*
[b] *Assistência Multidisciplinar em Oncologia (AMO), Salvador, BA, Brazil*
[c] *Instituto de Hematologia e Hemoterapia de Feira de Santana (IHEF), Feira de Santana, BA, Brazil*

ARTICLE INFO

Article history:
Received 20 February 2016
Accepted 21 September 2016
Available online xxx

Keywords:
Adult T-cell leukemia/lymphoma
ATL
Peripheral T-cell leukemia/lymphoma
Human T-cell lymphotropic virus type-1
HTLV-1 infection

ABSTRACT

Background: Adult T-cell leukemia/lymphoma is a peripheral disease associated with human T-cell lymphotropic virus type 1. Treatment is carried out according to clinical type with watchful waiting being recommended for less aggressive types. Aggressive adult T-cell leukemia/lymphoma is generally treated with chemotherapy and/or antivirals. The objective of this study was to correlate the survival of patients diagnosed in Bahia, Brazil, with the therapeutic approaches employed and to evaluate what issues existed in their treatment processes.

Methods: Eighty-three adult T-cell leukemia/lymphoma patients (26 smoldering, 23 chronic, 16 acute, 13 lymphoma and five primary cutaneous tumoral) with available data were included in this study.

Results: Complete response was achieved in seven smoldering patients with symptomatic treatment, in two with chronic disease using antivirals/chemotherapy, in one with acute disease using antivirals and in one lymphoma using the LSG15 regimen [vincristine, cyclophosphamide, doxorubicin, and prednisolone (VCAP); doxorubicin, ranimustine, and prednisolone (AMP); and vindesine, etoposide, carboplatin, and prednisolone (VECP)]. Smoldering patients who received symptomatic treatment presented longer survival. Favorable chronic patients treated with antivirals presented longer survival compared to the unfavorable subtype. However, for the acute form, first-line chemotherapy was better, albeit without significance, than antivirals. Only one of the patients with lymphoma and primary cutaneous tumors responded.

Conclusions: Watchful waiting associated with phototherapy represents the best option for smoldering adult T-cell leukemia/lymphoma with survival in Bahia being superior to that described in Japan. There was a trend of better results with zidovudine/interferon-alpha in

* *Corresponding author at*: Serviço de Dermatologia do Complexo HUPES, Ambulatório Magalhães Neto, 3° andar, Rua Padre Feijó, 240, Canela, 40110-170 Salvador, BA, Brazil.
E-mail address: pedrodermato@yahoo.com.br (P.D. Oliveira).

http://dx.doi.org/10.1016/j.bjhh.2016.09.012

Please cite this article in press as: Oliveira PD, et al. Adult T-cell leukemia/lymphoma treatment in Bahia, Brazil. Rev Bras Hematol Hemoter. 2016. http://dx.doi.org/10.1016/j.bjhh.2016.09.012

favorable chronic disease. Excellent results were achieved in the lymphoma type treated with the LSG15 protocol. Patients are diagnosed late probably due to lack of knowledge of adult T-cell leukemia/lymphoma by primary healthcare doctors and a Brazilian treatment protocol needs to be established.

Introduction

Human T-cell lymphotropic virus type 1 (HTLV-1) is endemic in southwestern Japan, sub-Saharan Africa, South America and the Caribbean with foci in the Middle East and Australo-Melanesia.[1] A seroprevalence study in the general population of Salvador, Bahia, Brazil showed a rate of 1.7% of HTLV-1 infected individuals.[2]

Although the majority of HTLV-1 carriers remain asymptomatic, around 10% develop serious diseases such as adult T-cell leukemia/lymphoma (ATL), HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP), HTLV-1-associated uveitis and infective dermatitis associated with HTLV-1 (IDH).[3] ATL is an aggressive lymphoproliferative disease of peripheral T cells characterized by short survival and a poor response to chemotherapy.[4]

Diagnostic criteria for ATL include positive serology for HTLV-1 and a histologically or cytologically proven peripheral T-cell malignancy. Whenever possible, the HTLV-1 proviral integration analysis should be performed, except in clinically and morphologically straightforward cases when it is unlikely that confirmation of HTLV-1 viral integration is necessary for diagnosis.[5,6] In endemic areas, it is rare that HTLV-1-associated lymphomas do not exist in seropositive patients.[5]

Due to diverse presentations, ATL is classified into five clinical types: smoldering, chronic, acute, primary cutaneous tumoral (PCT) and lymphoma (Table 1).[4,7]

The most aggressive forms of ATL are the acute, lymphoma, PCT and unfavorable chronic forms. Smoldering and the favorable chronic forms of ATL are less aggressive.[5]

Difficulty in the treatment of ATL is essentially due to chemotherapy resistance and the immune dysregulation caused by HTLV-1 infection making the patients more susceptible to other infections.[8,9]

The treatment is performed according to the clinical form. It is recommended to manage patients with less aggressive forms using supportive care, with a watchful waiting approach or antivirals with zidovudine (AZT) and interferon-alpha (IFN-α) being the most used. In aggressive ATL, patients are generally treated with chemotherapy, antivirals and/or bone marrow transplantation. Other treatment protocols are being tested such as monoclonal antibodies and arsenic trioxide.[5]

Objective

The aim of this study was to correlate survival with treatment approaches for the five different clinical types in Bahia, Brazil and to evaluate what issues existed in their treatment processes.

Methods

Patient characteristics

This was a cohort study of 83 ATL patients whose data were obtained in an ATL database of the Pathology Department of the University Hospital of the Universidade Federal da Bahia (UFBA). The majority of patients were diagnosed, treated and followed-up in the Hematology, Dermatology and Pathology Departments of the hospital. Most of these patients were dependent on the Brazilian National Health System (NHS), but 21 had health insurance plans and came from private hospitals or outpatient services of Salvador, Bahia for pathological reviews and study admission. Patients were diagnosed according to preexistent criteria.[5] In patients with more prolonged survival or with less than 19 years of age, HTLV-1 proviral integration was investigated using Southern blot or long-inverse polymerase chain reaction (PCR)[10,11] and all of them presented monoclonality. All patients were human immunodeficiency virus (HIV) negative.

Initially we had 101 patients diagnosed with ATL but 18 were ineligible for the study due to short survival or short treatment duration (< 1 month). Of the 83 selected patients, 55 lived in Salvador and 28 in the interior of Bahia. Mean disease duration (time elapsed from beginning of symptoms until diagnosis) was 24 months, 54.2% of patients were female, median age was 49.4 years (range: 9–84 years) and there was a predominance of Afro-descendants (88%). The study group was composed of 26 smoldering, 23 chronic (16 favorable and seven unfavorable), 16 acute, 13 lymphoma and five PCT patients. All the smoldering patients were non-leukemic, did not have pulmonary involvement and presented skin lesions. ATL association with HAM/TSP occurred in 14 patients (16.9%).

Treatment

Overall, 33 patients received first-line multiagent chemotherapy alone, 27 patients received first-line antiviral therapy alone, and four patients received chemotherapy associated to antiviral therapy as first-line therapy. Nineteen smoldering ATL patients were initially managed with watchful waiting, phototherapy, corticosteroids or radiotherapy. Phototherapy was made with narrow-band ultraviolet B (Nb-UVB) or psoralen and ultraviolet A (PUVA) applied 2–3 times per week, with an average of 109 sessions (minimum of 60 and

Please cite this article in press as: Oliveira PD, et al. Adult T-cell leukemia/lymphoma treatment in Bahia, Brazil. Rev Bras Hematol Hemoter. 2016. http://dx.doi.org/10.1016/j.bjhh.2016.09.012