CASE REPORT

Angioimmunoblastic T-cell lymphoma in elderly patient with a previous diagnosis of infectious mononucleosis: a challenge for cancer treatment – case report

Linfoma de células t angioimunoblástico em paciente idoso e com diagnóstico prévio de mononucleose infecciosa: um desafio para o tratamento oncológico – relato de caso

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ABSTRACT

Angioimmunoblastic T-cell lymphoma (AITL) is a rare subtype of peripheral T-cell lymphoma that represents about 2% of non-Hodgkin's lymphomas (LNH). It affects mainly men, in the sixth and seventh decades of life, and appears as a systemic disease. It has an aggressive behavior and responds poorly to chemotherapy, still with undefined standard treatment. This report aims to provide the poor prognosis in patients with AITL and the lack of treatment consolidation. The factors that may be associated with the poor response are being elderly, advanced stages, and constitutional symptoms.

Key words: Non-Hodgkin/drug therapy; Lymphoma, T-Cell, Peripheral; Lymphoma, Large-Cell, Immunoblastic; Infectious Mononucleosis.

RESUMO

O linfoma de células T angioimunoblástico (AITL) é subtipo raro de linfoma de células T periférico que representa cerca de 2% dos linfomas não Hodgkin (LNH). Acomete predominantemente homens, na sexta e sétima décadas de vida e se apresenta como doença sistêmica. É agressivo no comportamento e responde mal à quimioterapia, com tratamento padrão ainda não definido. Este relato objetiva apresentar o prognóstico desfavorável nos pacientes com AITL e a falta de consolidação de seu tratamento. Os fatores que podem estar associados à má-resposta são: idoso, estágios avançados e sintomatologia constitucional.

Palavras-chave: *Linfoma não Hodgkin/quimioterapia; Linfoma de Células T Periférico; Linfoma Imunoblástico de Células Grandes; Mononucleose Infecciosa.*

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INTRODUCTION

Angioimmunoblastic T-cell lymphoma (AITL) is a rare subtype of peripheral T-cell lymphoma, which represents about 2% of all non-Hodgkin lymphomas (LNH).[1,2] However, it occurs in about 16.8% of peripheral T cells lymphomas (PTCL), making it the most common type of this neoplasia.[1]

It affects mainly people in the sixth and seventh decades of life (mean age of 59-64 years old) and is usually presented as a systemic disease.[3] Its prevalent among men, with a male-female ratio of 2:1.[1,2]

AITL was initially described as angioimmunoblastic lymphadenopathy with dysproteinemia, and defined as a clinical syndrome characterized by generalized

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lymphadenopathy, hepatosplenomegaly, anemia, and hypergammaglobulinemia.[1,4] It has an aggressive behavior and responds poorly to chemotherapy. Some clinical features are similar to those of other lymphomas such as fatigue, lymphadenopathy, fever, night sweats, and weight loss, however, it is more often associated with: hepatosplenomegaly, anemia, hypergammaglobulinemia, hypereosinophilia,[5] cutaneous rash[6], and pleural bleeding.[1,7-10] AITL presents characteristics of autoimmune diseases such as autoimmune thrombocytopenia[1], autoimmune hemolytic anemia, polyclonal hypergammaglobulinemia, polyarthritis [6], and eosinophilia[1].

Despite the understanding of the biology of AILT, the prognosis is poor, with an overall survival of approximately 30% in five years, and a median survival of less than 26 months[8] in the conventional treatment. Treatment with high doses of chemotherapy associated with autologous stem cells (HDC/ACST) is associated with survival rates as: global over five years of 68%, and median high over 67 months.[9] The factors associated with poor results are not well-defined. The standard treatment has not been established, and response to treatment regimens is poor.[1]

This case report aims to help alert about this nosological entity, to understand better its evolution and attend to its diagnosis in many clinical situations.

CASE REPORT

AVS, leucoderma, 60 years old; developed fever, night sweats, significant and unintended weight loss, dry cough, generalized rash, asthenia, adynamia, and appetite loss, being admitted to the Santa Casa de Misericórdia of Belo Horizonte after a biopsy result of the right inguinal lymph node. Rash remission was observed with its evolution, however, showed edema of the lower limbs, ascites and dysuria. Identified cacifo sign (+++/4) and lymph adenomegaly: bilaterally cervical (2 cm), pre-auricular (3 cm), axillaries (5 and 6 cm), inguinal (4 cm), with fibroblastic consistency, movable, smooth and painless on palpation. Reduced lung sound was also observed in the infra-scapular region in both hemithorax, hepatomegaly at 6 cm from the right costal margin, and splenomegaly – Boyd: 4.

The previous diagnosis was infectious mononucleosis (12/12/2011: mono test: reagent, 12/30/2011 – Epstein serology: IgG: 123 (reagent), IgM: 24.4 (undetermined).

Hyperglobulinemia and grade IV neutropenia were identified. A chest X-ray revealed bilateral diffuse reticular consolidations, a suggestive pattern of cephalization with pulmonary flow/congestion. Computed tomography of the abdomen and pelvis showed a volumetric increase of liver and spleen, generalized lymphadenopathy in celiac chains, superior and inferior mesenteric, pre-aortic, para-aortic, cava intra-aortic, common iliac, internal and external, and bilaterally inguinal.

The histopathological analysis of the right inguinal lymph node biopsy was suggestive of diffuse small cell lymphoma, and the biopsy of the iliac crest revealed bone marrow fragments with increased cellularity compared to the myeloid tissue. There was a proliferation of cells with enlarged nuclei with interstitial monomorphic group pattern. Immunohistochemistry performed on 03.08.12 revealed that it was an angioimmunoblastic T-cell lymphoma, Ki-67 positive in the amount of 70% (high), and CD4 and CD8 positive. Presented positive granzyme B, proliferation of post-capillary venules associated with lymphoid proliferation and sometimes large T lymphoid cells of the immune-phenotype B (CD20 +).

The first cycle of chemotherapy was immediately started with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP), however, without a positive response. Additionally, cefepime was prescribed due to persistent fever; and furosemide for the worsening of systemic edema. Presented toxicity and side effects of the chemotherapy cycle with grade II anemia, grade IV neutropenia and grade I thrombocytopenia; the patient's death was associated with persistent refractory acute peripheral circulatory failure to treatment.

DISCUSSION

AITL is a rare type of peripheral T-cell lymphoma with poor prognosis. The diagnosis is more common in the age group of 59-65 years (ranging from 27-90 years), especially in men. In 67.7% of patients, the observed staging is located in Ann Arbor III or IV; 58.1% present B symptoms (sweating, weight loss, and fever); 48.8% demonstrate hypoalbuminemia (<35 g/L), and 63.3% presents high lactate dehydrogenase content (LDH) upon diagnosis.[1] In this case, the patient was a 60 years old male who reported B symptoms.

In this report, infectious mononucleosis was previously diagnosed, however, the relationship between

AITL and Epstein-Barr (EBV) virus was identified in several reports, without determining difference in the overall survival, whether in patients with AITL who were EBV carriers or not.[1] There are reports, however, of three patients with T-cell lymphoma, fatal, with some abnormalities involving high titers of antiEBV antibodies and tumor cells containing the EBV genome. This suggests that EBV can infect T cells and contribute to the development of lymphoma.

The factors that most influence the overall survival of patients according to the multivariate analysis are: initial presentation with fever, advanced stage, and treatment without complete remission. Most study patients received cyclophosphamide, vincristine, and prednisone or cyclophosphamide, doxorubicin, vincristine, and prednisone (COP/CHOP). There was no difference in the overall survival between the schemes with or without anthracycline. In the study, 28% of patients achieved a complete response to treatment and 72% did not. Survival of two years in the first group of patients was 87.5% against 20% in the second group. The median survival was 14.9 months. The overall survival at follow-up of one, two, three, and five years was 54.8, 41.9, 35.5, and 12.9%, respectively. Most of the deaths that occurred during the study follow-up were due to active disease (77.4%).

Bone marrow transplantation is an alternative therapy since the Parma[11] randomized study determined convincingly that a high dose chemotherapy-associated autologous stem cells (HDC/ACST) is the best recovery therapy for patients with chemo-sensitive diseases in the intermediate level of the Working Formulation of non-Hodgkin lymphomas group (NHL).

Thus, to provide information on these issues, the Spanish Lymphomas /Autologous Bone Marrow Transplant Group (GEL-TAMQ) described the experience with 115 patients with peripheral T cells lymphoma (PTCL) classified according to the European-American Review Lymphoma (REAL) submitted to HDC/ASCT. According to the results: out of the 114 patients, 98, six, three, and seven achieved complete remission, partial remission, stable disease, and progressive disease, respectively. The follow-up median was 37 months in 63% of alive patients, and estimated five-year survival rate in 56%; 60% of the patients achieved complete remission with free of disease survival. In this study, one patient died of myelodysplastic syndrome.

There are few studies available using HDC/ASCT as the first therapeutic option. However, therapy with this regimen demonstrated a significant number of patients who achieved complete clinical remission compared with only conventional chemotherapy for aggressive lymphomas.[11-19]

CONCLUSION

It can be concluded that AITL is rare. However, it remains as an aggressive disease with poor prognosis even with the most recommended treatment, i.e., COP/CHOP. The factors that may be associated with poor prognosis are: elderly patients, advanced stages, poor general condition, constitutional symptoms, and systemic involvement. The overall five-year survival was approximately 30%, with a median survival of fewer than 26 months.

Treatment with high-dose chemotherapy associated with autologous stem cells (HDC/ACST) was associated with better outcome compared to just chemotherapy.[11,12] However, peripheral T cells lymphomas still do not present well–defined results.

Other treatment regimens should be investigated in order to find and consolidate a standard treatment allowing better prognosis, with overall survival and longer disease-free survival.

This report presents the severity of this form of anatomo-clinical presentation of non-Hodgkin lymphomas, which diagnosis should be considered, especially in elderly patients with generalized lymphadenopathy, hepatosplenomegaly, anemia, hypergammaglobulinemia, eosinophilia, weight loss, rash, characteristics of autoimmune diseases, aggressive behavior, and poor response to chemotherapy.

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