

Soft-tissue masses as presentation of non-Hodgkin's lymphoma in AIDS patients*

Massas de tecidos moles como apresentação do linfoma não-Hodgkin em pacientes com AIDS

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Abstract: Primary soft tissue Non-Hodgkin lymphomas are very rare and account only for 0.1 % of the cases. Generally, Non-Hodgkin lymphomas of the soft tissue present as large subcutaneous masses without evidence of nodal or skin involvement. We describe four cases of primary Non-Hodgkin lymphomas of the soft tissue in patients infected with the human immunodeficiency virus. The most common site of involvement was the chest wall in all the patients; histopathological and immunophenotypic examination of the biopsy smears revealed two cases of plasmablastic lymphomas, one Burkitt and one diffuse large B-cell lymphoma. Non-Hodgkin lymphomas should be included in the differential diagnosis of soft tissue masses in human immunodeficiency virus - seropositive patients.

Keywords: Acquired immunodeficiency syndrome; HIV; Lymphoma, B-Cell; Lymphoma, Non-Hodgkin; Soft tissue neoplasms

Resumo: Os linfomas Não-Hodgkin primários de tecidos moles são muito raros e responsáveis por somente 0,1% dos casos. Geralmente, os linfomas Não-Hodgkin de tecidos moles se apresentam como massas subcutâneas sem evidência de comprometimento dos nódulos ou da pele. Descrevemos aqui quatro casos de linfomas Não-Hodgkin primário de tecidos moles em pacientes infectados pelo vírus da imunodeficiência humana. O local mais comum de comprometimento foi a parede torácica em todos os pacientes; os exames histopatológico e imunofenotípico do esfregaço da biópsia revelaram dois casos de linfoma plasmablástico, um linfoma de Burkitt e um linfoma difuso de grandes células B. O linfoma Não-Hodgkin deve ser incluído no diagnóstico diferencial de massas de tecidos moles nos pacientes soropositivos para vírus da imunodeficiência humana.

Palavras-chave: HIV; Linfoma de células B; Linfoma não Hodgkin; Neoplasias de tecidos moles; Síndrome de imunodeficiência adquirida

INTRODUCTION

The risk of developing lymphomas is greatly increased in HIV infected patients. AIDS associated lymphomas are characterized by their rapid progression, frequent extranodal initial manifestations and poor outcome.¹ The incidence of extranodal non-Hodgkin's lymphomas (NHL) in HIV/AIDS patients

is 3%; soft tissue involvement is rare and is described only in 0.1% of the cases.¹ In this article, we reviewed the epidemiological, clinical, histopathological, immunological, virological and the outcome of four HIV/AIDS patients with soft tissue masses as clinical presentation of NHL.

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CASE REPORT

The patients were clinically staged according to the Ann Arbor system. Primary NHL of the soft tissue was defined as those lymphomas presenting with involvement of the soft tissue or the muscle as the predominant manifestation of the disease. Patients with cutaneous or bone tissue involvement were excluded. All diagnoses were performed by histopathological examination of biopsy smears obtained from the soft tissue masses. Histopathological diagnosis was made according to the criteria of the World Health Organization (WHO).² Immunohistochemical stains were applied in all cases. During an 11-year period analyzed in our hospital for infectious diseases, 92 HIV-infected patients were diagnosed with lymphoma. Sixty-six (72%) of them had NHL and 26 (28%) had Hodgkin's disease. Of 66 NHL, 41 (64%) were extranodal NHL and 4 (0.09%) were soft tissue primary NHL. All were males with a median of age of 41 years. Clinical presentation showed painless and large subcutaneous masses with rapidly increasing size. Two patients with history of intravenous drug use (IVDUs) had antibodies against hepatitis C virus (HCV) and the other 2 presented positive hepatitis B (HBV) serology. Lactate dehydrogenase (LDH) levels were elevated in the 4 patients and only one patient (25%) had evidence of bone marrow infiltration. Sites of involvement included the chest wall in all of them (Figures 1 and 2) with other masses in the upper leg and the scalp in two. Histopathological and immunophenotype studies revealed 2 plasmablastic lymphomas (PBL), 1 diffuse large B cell lymphoma (DLBCL) and 1 Burkitt lymphoma (BL). Two patients died after a short survival time following lymphoma diagnosis due to an aggressive and rapid clinical course of the neoplasm and disseminated tuberculosis, respectively, without the possibility of receiving chemotherapy because of his poor clinical status. One patient died 12 months later of unrelated cause and the other is alive. Demographic and clinical findings are summarized in tables 1 and 2.

DISCUSSION

The incidence of NHL including DLBCL, Burkitt's lymphoma and PBL is increased among HIV-seropositive patients and 16% of deaths in AIDS patients have been associated with lymphomas.² The incidence of NHL in HIV patients is 3% and the lesions usually are of high-grade and with extranodal involvement as clinical presentation. About 70% of AIDS-associated lymphomas are NHL.^{1,2} The incidence of extranodal NHL of the soft tissues is low and account only for 0.1% of the cases.^{3,4} Soft tissue lymphomas at presentation are considered to be primary only if the staging procedures exclude other disease sites.³ Soft tissue

lymphomas include those masses that involve the subcutaneous and the musculoskeletal tissues; in our experience, these neoplasms are characterized by fast growth with frequent involvement of the adjacent tissues, such as the skin and bone (Figure 3).³



FIGURE 1: A large mass involving soft tissues in the chest wall, without compromising the skin or axillary lymphadenopathy



FIGURE 2: A subcutaneous tumor located on the chest wall.



FIGURE 3: A large soft tissue mass involving the subcutaneous and musculoskeletal tissue on the chest wall. There is no evidence of regional nodal infiltration.

TABLE 1: Demographic findings in four cases of soft tissue lymphomas from AIDS patients

	1	2	3	4
Gender	male	male	male	male
Age	35	46	37	48
HIV/risk infection	IVDUs	IVDUs	Unprotected sexual contact	Unprotected sexual contact
Clinical Stage	Advanced	Advanced	Advanced	Advanced
HBV	(-)	(-)	(+)	(+)
HCV	(+)	(+)	(-)	(-)
LDH (U/L)	1280	786	926	1518
Bone marrow involvement	(+)	(-)	(-)	(-)

IVDUs: Intravenous drug users

TABLE 2: Immunological, histopathological and virological findings from AIDS patients with soft tissue lymphomas

	1	2	3	4
Location	Chest wall and upper leg	Chest wall	Chest wall, scalp	Chest wall
CD4 level (cell/uL)	37	357	56	201
Plasma Viral Load	Detectable	Undetectable	Detectable	Undetectable
Histological subtype	Plasmablastic lymphoma	Diffuse large B cell lymphoma (DLBCL)	Plasmablastic lymphoma	Burkitt's lymphoma
Survival	1 month	6 months	1 month	12 months
Treatment	None	CHOP-R plus HAART	none	CHOP-R plus HAART
Response	None	Partial	None	Partial
Cause of death	Lymphoma progression	Alive	Disseminated tuberculosis	Sepsis with multiorgan failure

Salamao et al describes a clinic pathologic study of 19 patients who developed lymphomas as soft tissue masses without evidence of lymph node involvement.⁴ The authors conclude that malignant lymphomas initially diagnosed in soft tissues are most commonly DLBCL. In contrast, 2 patients of our series had diagnosis of the histopathological subtype named as PBL. These are rare tumors occurring almost exclusively in the setting of HIV infection. PBL was recognized as a distinct entity, a subtype of DLBCL, in the World Health Organization (WHO) classification; one was a BL and the last was a DLBCL.^{5,6}

Cutaneous B-cell lymphomas have been also described in HIV patients as red skin nodules in the arms, head and trunk. These lesions usually start in the skin and may involve subcutaneous tissues.⁷

In our experience, ultrasound of musculoskeletal tissue provides valuable information about the extent of the mass.^{8,9}

Advanced neoplasm disease at presentation, bone marrow infiltration, prior diagnosis of AIDS and a poor performance status are associated with a shorter survival in HIV-patients associated NHL, as we can see in our series.¹⁰

Early excision biopsy is necessary to confirm the diagnosis of these neoplasms and to determine the histopathological subtype.

Chemotherapy and/or radiotherapy are the best therapeutic alternatives for NHL of the soft tissues; however, some authors have published a good clinical outcome in patients treated with a wide surgical excision followed by chemotherapy.⁹

The impact of highly active antiretroviral therapy (HAART) on NHL response and survival rates has been well demonstrated in several studies. Patients receiving HAART plus chemotherapy have a more significant opportunity to achieve complete remission.¹⁰ In our series, the 2 patients treated with chemotherapy plus HAART had a partial clinical response.

Early diagnosis followed by chemotherapy plus HAART is necessary to achieve a good clinical outcome in this kind of patients. □

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