CASE REPORT

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AIDS-related lymphoma in a young HIV late presenter patient

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Abstract

Non-Hodgkin's lymphoma (NHL) is an acquired immunodeficiency syndrome (AIDS)-indicative disease. Nowadays, NHL is rarely reported in Europe as indicative disease for human immunodeficiency virus (HIV) testing. We present the case of a 22-year-old Romanian male patient without past medical history, except the swelling of a submental lymph node 11 months ago. The excised node was histologically examined but the patient neglected to take his result. He was admitted for fever, asthenia, and weight loss over 10% of his weight, and night sweats in the last four months. The immunohistochemical analysis of the preserved lymph node samples suggested reactive hyperplasic lymphadenitis with suppuration and necrosis (lymphoid follicles CD20+, CD10+, BCL6+; germinal centers CD23+, CD68+, Ki67+; and interfollicular CD3+). Clinical, biological and imaging evaluations were performed. The diagnostic of lymphoma stage IV Ann Arbor was sustained. Severe immunosuppression and a positive HIV test were found. The patient received antiretroviral treatment, but he developed paraplegia consecutive to a vertebral metastasis, liver and kidney failure and died sooner than two months from the diagnostic time. Pathological examination confirmed NHL with diffuse lymphocyte infiltrate of multiple organs. Advanced lymphoma is a rare indicator condition of HIV diagnostic. Delayed diagnostic of lymphoma implies ethical issues on communication deficiencies between the heath providers and patients, concerning the significance of biopsy. Infectious co-morbidities with necrosis and suppurative lesions are confounder conditions in NHL histological and immunohistochemical diagnosis.

Keywords: AIDS-related, lymphoma, non-Hodgkin's.

Introduction

In 2012, there were 93 433 persons diagnosed with non-Hodgkin's lymphoma (NHL) and 37 861 deaths were recorded with this diagnosis in the European countries [1]. At the same time, there were recorded 29 381 new human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) cases and 1583 deaths. Nowadays, non-Hodgkin's lymphoma is an AIDS defining disease [2], although it is a rare indicator for HIV diagnosis in Europe [3].

The epidemiology of HIV/AIDS associated malignancies has been changed in recent years. Before the use of antiretroviral therapy (ART), 10% of HIV-associated deaths were caused by neoplasms, especially AIDS-related cancers, such as Kaposi's sarcoma, non-Hodgkin's lymphoma and invasive cervical carcinoma [4, 5]. Systematic ART significantly improved the life expectancy of HIV-infected patients, along with the decline of mortality due to AIDS-defining cancers, while non-AIDS cancers and other non-neoplastic diseases are increasing [6]. However, present incidence of HIV-associated lymphomas remains higher than in the non-HIV population [7].

The aim of this report is to present a case of non-Hodgkin's lymphoma in a very late presenter young patient with HIV infection. We discuss the clinical, biological and imagistic presentations, corresponding to the immunohistological data.

Case presentation

We present the case of a young man from Romania, aged 22, living in a rural area, hospitalized for progressive disease in the last four months. He presented with fever, fatigue, weight loss >10%, diarrhea, night sweats and fatigue. The patient had an educational level of 10 years, denied alcohol consumption and smoking. He started his sexual life at the age of 15 years, had multiple partners, and at the moment has a stable relationship. He was not employed, but he worked in Italy for one year. The medical history was insignificant, except for the excision of a submental lymph node (1×2 cm), 11 months earlier.

The clinical exam revealed fever 38.2^{0}C, respiratory rate 24/min., heart rate 124/min., blood pressure 100/70 mmHg, weight 52 kg, height 175 cm, hepatomegaly, splenomegaly. There were no lung crackles, rash, meningeal syndrome or focal neurological signs found. The initial evaluation revealed severe anemia, leucopenia, thrombocytopenia and inflammatory biological syndrome. Hematological malignancy was suspected and the histological sample of the lymph node excised 11 months ago was retrieved. The microscopic examination identified follicular hyperplasia with large cells, areas of necrosis and suppuration. Immunohistochemical analysis evidenced CD20+, CD10+, BCL6+ in lymphoid follicles, CD23+, CD68+, Ki67+ in germinal centers and CD3+ interfollicular. The diagnosis of reactive hyperplasic lymphadenitis and suppurative necrosis was considered.

Computer tomography (CT) of the brain was normal, while thoracic and abdominal sections evidenced aorto-pulmonary and retroperitoneal lymph nodes, bone lysis of the T9 body vertebra spongiosa (Figures 1 and 2). Multiple nodules with central hypodensity and weak uptake of iodine dye in the periphery were found in the liver (Φ 6 mm, Φ 49 mm, Φ 59 mm) and spleen (Φ 29 mm – Figures 3 and 4).

The viral markers for hepatitis B and C viruses were negative, but positive for HIV (ELISA and Western Blot tests). The lymphocyte count was LTh (CD3 + CD4) 15/mm^3 (2.2%) and LTs (CD3 + CD8) 595/mm^3, with LTh/LTs 0.003. The exam of cerebrospinal fluid (CSF) was normal and the level of lactate dehydrogenase (LDH) was markedly elevated – ×10 NV (normal value). Severely compromised immunity and criteria diagnostic for lymphoma justify the classification C3 AIDS and urgently initiation of ART. Deferring the cancer therapy was decided in the context of irrelevant immunohistochemical retrospective examination, the refusal of bone marrow biopsy and poor biological status. We expected to improve the immune status under ART but the patient returned after three weeks with hyperalgesia syndrome due to thoracic vertebral compression (T9), which rapidly evolved into paraparesis, bowel and bladder paresis, anasarca, liver failure, kidney failure and, in the end, death. Pathological examination confirmed the presence of multinodular tumors in the liver, spleen, mesenteric, peritoneal and retroperitoneal lymph nodes (Figures 5–7). Microscopic examination confirmed the presence of diffuse lymphocytic infiltrates with large cells in the liver, spleen, kidneys and lymph nodes, compatible with non-Hodgkin's lymphoma (Figures 8–10).

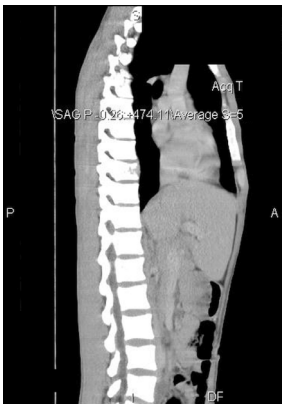

Figure 1 – ***Thoracic CT+C – transversal scan plan: Anterior and superior diffuse hypodense bone image in T9 vertebral body.***

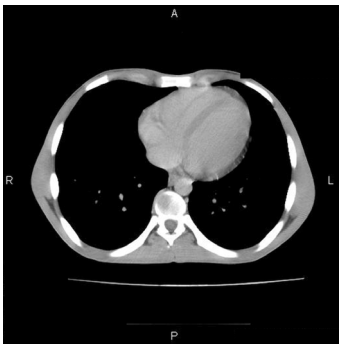

Figure 2 – ***Thoracic CT+C – transversal scan plan: Anterior and superior diffuse hypodense bone image in T9 vertebral body.***

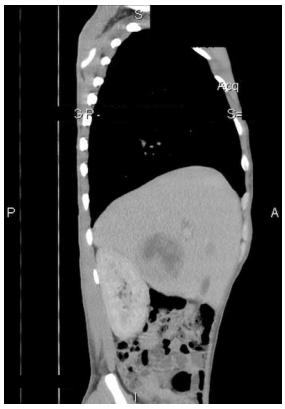

Figure 3 – ***Abdomen CT+C – coronal scan plan: Heterogeneous nodular liver images with hypodense center and peripheral low enhancement.***

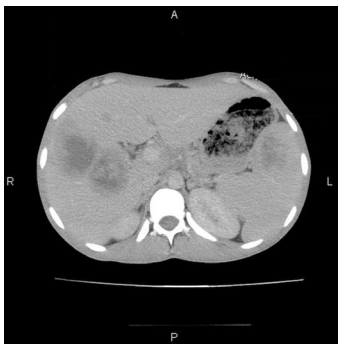

Figure 4 – ***Abdomen CT+C – transversal scan plan. Heterogeneous nodular liver images with hypodense center and peripheral low enhancement.***

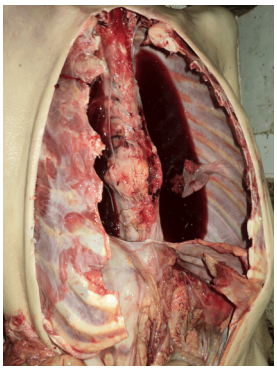

Figure 5 – ***Bilateral hemothorax; T9 paraspinal mass – physical appearance.***

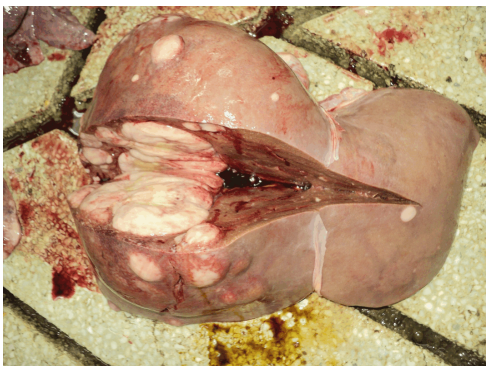

Figure 6 – ***Multinodular tumors of the liver – physical appearance.***

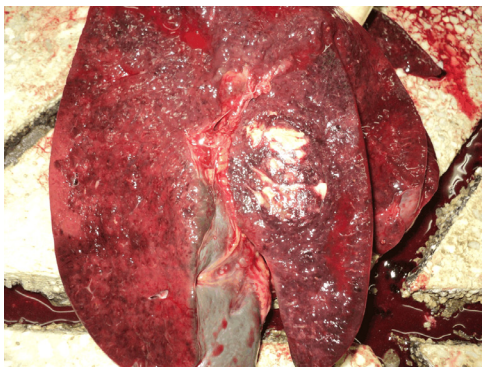

Figure 7 – ***Nodular tumor of the spleen – physical appearance.***

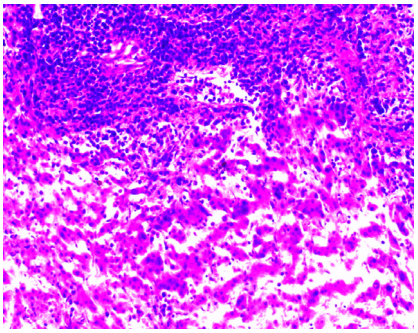

Figure 8 – ***Lymphocyte infiltrates involving sinusoidal spaces of spleen (HE staining, ×100).***

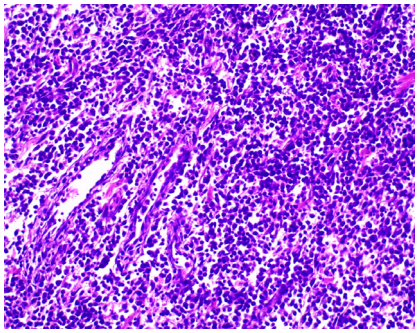

Figure 9 – ***Lymphocyte infiltrates involving sinusoidal spaces of spleen (HE staining, ×100).***

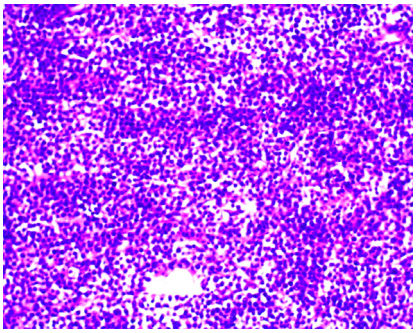

Figure 10 – ***Lymph node in T9 vertebrae with lymphocytic infiltrates (HE staining, ×100).***

Discussion

The patient was a young man from Romania. His age was close to pediatric cohort (1988–1990) with HIV nosocomial epidemic, although the patient's history was not relevant for transfusions, hospitalization or parenteral treatments. Heterosexual HIV transmission is possible, given the multiple sexual partners, although his stable female partner was negative for HIV ELISA test. The peculiarity of the case is the association of lymphoma with HIV infection in a severely immunossupressed stage. The diagnosis was late, because the patient did not understand the importance of the biopsy and he neglected the outcome of this investigation. Testing for HIV, according to the testing guidelines was recommended in the context of the diagnosis of lymphoma, which is one of the AIDS-indicator conditions [8]. The histological description of the biopsy sample from lymph node prevailed a few months earlier was different in comparison with the diffuse infiltrate mentioned in the autopsy, suggesting the possible transformation of an initially follicular lymphoma into a diffuse large cell lymphoma with aggressive evolution, favored by the decline of immunity. This transformation process can occur in 25–60% of patients with follicular lymphoma [9]. The immunohistochemical investigations are expensive and difficult to be achieved. The low economical level of the patient, limited the access to some medical services. Comparison of the immunohistochemical profile of the biopsy samples and necropsy samples was not affordable. Available immunohistochemical result did not support the diagnosis of lymphoma. Immunohistochemical examination errors may have been caused by improper technique accuracy or inadequate quality of examined samples. Moreover, the necrotic tissue described in the initial lymph node samples could have distorted the histological results. For example, the proliferative activity expressed by Ki67 may have been underestimated, or the markers for T-cells may have been false positive [10].

Necrosis is found both in inflammatory reactions and in lymphomas, poorly or well differentiated. The necrosis may indicate mycobacterium or fungal infections that can be associated lymphoma, explaining the diagnostic failure of the malignant disease. Prognostic significance of immunohistochemical markers for lymphoma and diffuse large B-cells are evaluated by several algorithms, but the results are controversial. The concordance between the results of different methods of diagnosis of non-Hodgkin's lymphomas is estimated at 88% [11, 12].

The stage of lymphoma considered was based on medical history, clinical examination, laboratory investigations and imaging. Severely altered biological status at the time of lymphoma diagnosis explains the strategy of sequential initiation of treatments, firstly antiretrovirals and secondly oncological treatment, after the improvement of immunity.

The frequency of spinal localization of NHL is 0.1–6.5% of cases [13, 14].

The spinal cord compression in our patient was consequent to the fast dissemination of NHL, before the decision of radio or chemotherapy. Survival and prognosis of patients with non-Hodgkin's lymphoma associated with HIV were evaluated in an observational study that included 847 patients from 30 European countries, of which 763 had systemic forms. *Collaboration of Observational HIV Epidemiological Research Europe* (COHERE) study mentioned the proportion of histological forms of lymphoma: Burkitt's lymphoma 10%, lymphoma with diffuse large cells 8% and unspecified or other types 82%. The characteristics of the patients at the time of lymphoma diagnosis were: median age 41.2 years, 82% male, 43% not receiving ART and median CD4 150/mm^3. Lymphoma and HIV infection were simultaneous diagnosis in 13% of cases. Two-thirds of the patients diagnosed with HIV-associated lymphoma survived more than one year. Severe immunosuppression was the most important risk factor for death [15]. Comparative with COHERE study, our patient was younger, expressed dramatically lower immunity and survived less than two months after diagnosis.

Conclusions

A severe form of lymphoma in a young man was diagnosed as indicator of immunosuppression of advanced HIV infection. Deferring the diagnosis of lymphoma was the consequence of inadequate communication between the healthcare provider and patient concerning the importance of biopsy results. A multidisciplinary medical team is required for the complex processing of clinical, imaging and laboratory criteria for the diagnostic of lymphoma.

Conflict of interests

The authors declare that they have no conflict of interests.

Informed consent

Written informed consent was obtained from the patient for this case report and any accompanying images. His family approved the publication of the report after he died.

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