

NON-HODGKIN LYMPHOMA WITH FULMINANT EVOLUTION IN A PATIENT WITH HIV INFECTION INITIALLY IN STAGE A3 – CASE PRESENTATION

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ABSTRACT

HIV infection is associated with an increased risk for the development of hematological malignancies, especially non-Hodgkin lymphoma (NHL), which continues to present aggressive forms despite therapeutic advances.

We present the case of a 49-year-old patient, originally from Ukraine, diagnosed in January 2023 with HIV infection stage A3 according to the Centers for Disease Control and Prevention (CDC) classification. Clinical, paraclinical and histopathological data were retrospectively analyzed to highlight evolutionary and therapeutic peculiarities.

Although the patient promptly initiated antiretroviral therapy (ART), the oncological risk associated with persistent immunosuppression remains significant, according to data in the literature. Eleven months after the diagnosis of HIV infection, he developed systemic symptoms, and investigations confirmed the presence of an aggressive NHL, an entity described as being among the most common HIV-associated malignancies. Despite the rapid institution of specific treatment, the evolution was fulminant, with progressive deterioration and death, a scenario also documented in other cases of aggressive NHL associated with immunosuppression.

This case reflects the severe evolutionary potential of NHL in HIV patients, even in early stages of infection. Early identification of symptoms, prompt evaluation and multidisciplinary management are crucial to improve prognosis, according to international recommendations.

Keywords: HIV, non-Hodgkin lymphoma, immunosuppression, fulminant evolution, case report

Introduction

Human immunodeficiency virus (HIV) infection remains a major public health problem worldwide, despite significant advances in early diagnosis and combination antiretroviral therapy (ART). Although ART has transformed HIV infection into a manageable chronic disease, infected patients continue to be at increased risk for developing malignancies, particularly hematological malignancies. Among these, non-Hodgkin lymphoma (NHL) is one of the most common and severe HIV-associated malignancies and is considered a defining condition of AIDS

(1-4).

The mechanisms involved in the pathogenesis of NHL in HIV patients are complex and multifactorial, including profound immunosuppression, chronic immune activation, viral coinfections (especially Epstein-Barr virus). Even in the era of ART, HIV-associated NHLs tend to have an aggressive biological behavior, with atypical clinical presentation, rapid dissemination and a poor prognosis (5-8).

Diffuse large B-cell lymphoma is the most common histological subtype of NHL found in HIV-infected patients, often diagnosed at advanced stages, with extensive involvement,

including the gastrointestinal tract, liver, spleen, or central nervous system (6,9,10). Despite virological control achieved with ART and progressive increase in CD4 lymphocyte count, the oncological risk is not completely eliminated while the evolution can be rapidly progressive and fulminant (7,11).

The purpose of this case report is to highlight the clinical, imaging and histopathological features of an aggressive NHL in an HIV-infected patient on antiretroviral therapy, with an apparently favorable viro-immunological response. The case highlights the need for increased clinical vigilance, rapid multidisciplinary evaluation and the importance of early diagnosis in improving the prognosis of these patients.

Case presentation

Patient, 49 years old, known to have HIV infection since January 2023 (at initial evaluation CD4= 46 cells/mm³, HIV-RNA= 1,160,000 copies/ml) and under ART, chronic hepatitis with hepatitis C virus, negative anti-Epstein-Barr IgM antibody, positive anti-Epstein-Barr IgG antibody, presented in October 2023 for admission to the Clinical Hospital for Infectious Diseases in Constanța for symptoms with onset in August 2023 represented by epigastric pain and significant weight loss (9 kg in 3 months).

The clinical examination upon admission reveals relatively good general condition, the patient is conscious, cooperative, afebrile, with normal sclero-tegumentary coloration and decreased appetite, affirmative anamnesis reported by the patient. On palpation, bilateral cervical and axillary adenopathies and adenopathic blocks are observed, with diameters between 2–10 cm: submandibular ≈2 cm, supraclavicular ≈2 cm, bilateral axillary 2–10 cm, hard, mobile, painless. The examination of the digestive system reveals a painless abdomen spontaneously and on palpation, a non-palpable spleen, a liver with its lower edge 1 cm below the costal margin. The heart sounds are rhythmic, without stethoacoustically detectable murmurs, BP=120/80 mmHg, VA=86 bpm, bilateral symmetrical peripheral pulse. Otherwise, the

objective examination of the organs and systems is within normal limits.

Upon admission, it was decided to perform several investigations. The imaging included CT of the thoraco-abdominal and pelvis, abdominal MRI and brain CT. The CT of the thoraco-abdominal revealed hepatomegaly associated with multiple well-demarcated nodular formations at the hepatic level, as well as splenic lesions suggestive of secondary determinations, without pelvic adenopathies. The abdominal MRI, performed natively and post-contrast, confirmed the presence of multiple hepatic lesions, with T2 hypersignal, diffusion restriction and discrete peripheral contrast uptake, without dilatation of the intrahepatic bile ducts, aspects suggestive of secondary hepatic damage. The other abdominal organs (pancreas, kidneys, adrenal glands) did not present significant changes. On brain CT, an isodense tissue formation was revealed at the level of the left maxillary sinus, with extension into the nasal fossa and oropharynx, associated with bilateral laterocervical adenopathies, suggestive of lymphoproliferative damage.

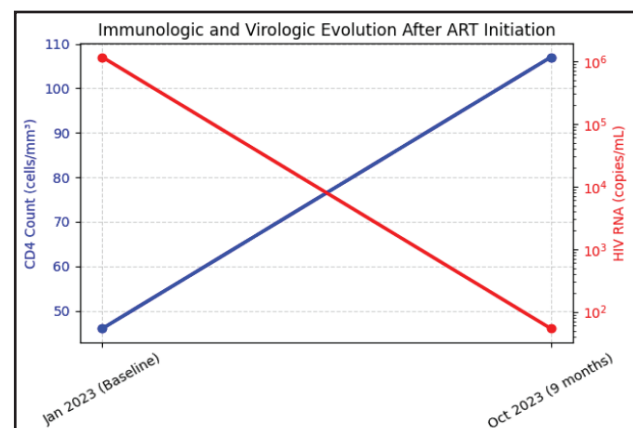


Figure 1: Evolution of immunovirological parameters under antiretroviral therapy, showing a significant increase in CD4 lymphocyte count (from 46 to 107 cells/mm³) and a marked decrease in HIV viral load (from 1,160,000 to <20 copies/ml) over a 9-month period.

Given the patient's known history of HIV infection, it was vital to assess the patient to get an idea of the evolution of the disease under antiretroviral treatment. The assessment includes CD4 lymphocytes and viral load (HIV-RNA) shown in the graph (Figure 1). Correct and continuous administration of ART is the central element in the management of patients with

HIV infection, as it contributes to increasing the number of CD4 lymphocytes and decreasing HIV-RNA.

Serological data are obtained revealing CD4=107 cells/mm³ and HIV RNA <20 copies/ml, highlighting the favorable viro-immunological evolution under ART. PET CT is performed: expansive hypercapturing formation for F18-FDG developed in the cavum, oro - and hypopharynx; the lesion extends bilaterally parapharyngeal, infiltrates the clivus, the tip of the left temporal bone, the sphenoid, extends into the left maxillary sinus and into the posterior ethmoidal cells, obstructing the left nasal fossa. Normal radiotracer uptake in the structures of the larynx, salivary glands and thyroid gland. Images of intensely F18-FDG-positive adenopathies, located: bilateral submandibular, in all bilateral cervical lymph node stations (maximum 5.2/2.3 cm and SUV (Standardized Uptake Value) up to 24.32 - on the left, respectively maximum 5.3/3.3 cm and SUV up to 26.63 on the right side), supraclavicular, retropectoral, bilateral axillary (maximum 2.4/2.4 cm and SUV up to 26.69 - on the right), prevascular and right paratracheal (maximum 2.2/1.5 cm and SUV up to 14.84 - prevascular). Subdiaphragmatically, metabolically active adenopathies are highlighted, located: celiomesenteric, hepatic hilar, interportocava and left inguinal-femoral, with dimensions of maximum 2.4/2.2 cm and SUV up to 25.50 (hepatic hilar). Both lungs are without metabolically active nodular lesions. Plaques of left posterior pachypleuritis.

F18-FDG hyperfixing tumor formation, developed at the level of the gastric fornix and in the vertical portion, with SUV 14.48. Metabolically active, spontaneously hypodense lesion, located in hepatic segment VII, with diameters of 1.8/1.3 cm and SUV 4.06. Hypodense lesions (at least two) in the splenic parenchyma, hyperuptake for radiotracer, with SUV up to 9.42. Pancreas, gallbladder and adrenal glands with normal morphological appearance on native CT examination, without metabolically active lesions. At the level of a jejunal loop in the left hypochondrium - flank, a concentric thickening of 1.6 cm is noted, extending over at least 6 cm; the lesion is intensely fixative for the radiotracer, with SUV 13.84. Normal uptake of the radiotracer

at the level of the colic frame. Physiological excretion of F18-FDG in the kidneys and urinary bladder. Left renal inferior calyx microcalculus. Prostate without metabolically active lesions on PET-CT examination with F18-FDG. Seminal vesicles and testicles of normal conformation, with physiological uptake of the radiotracer. No foci with pathological uptake of F18-FDG in the scanned bone segments; degenerative vertebral changes in layers. Osteocondensing lesion located on the left iliac wing, metabolically inactive. (Figure 2; Figure 3)

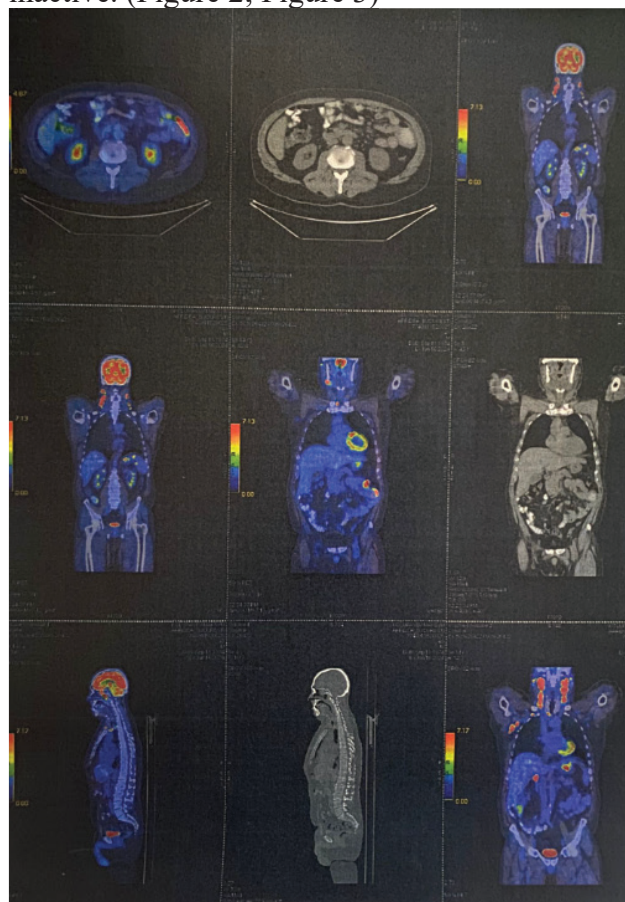


Figure 2: F18-FDG PET-CT scan demonstrating multiple areas of intense radiotracer uptake involving thoracic, abdominal and pelvic lymph node stations, as well as extranodal sites, suggestive of disseminated aggressive lymphoproliferative disease

The set of imaging investigations indicated a disseminated lymphoproliferative disease, with multiple nodal and extranodal involvement, suggesting an aggressive biological nature of the pathological process.

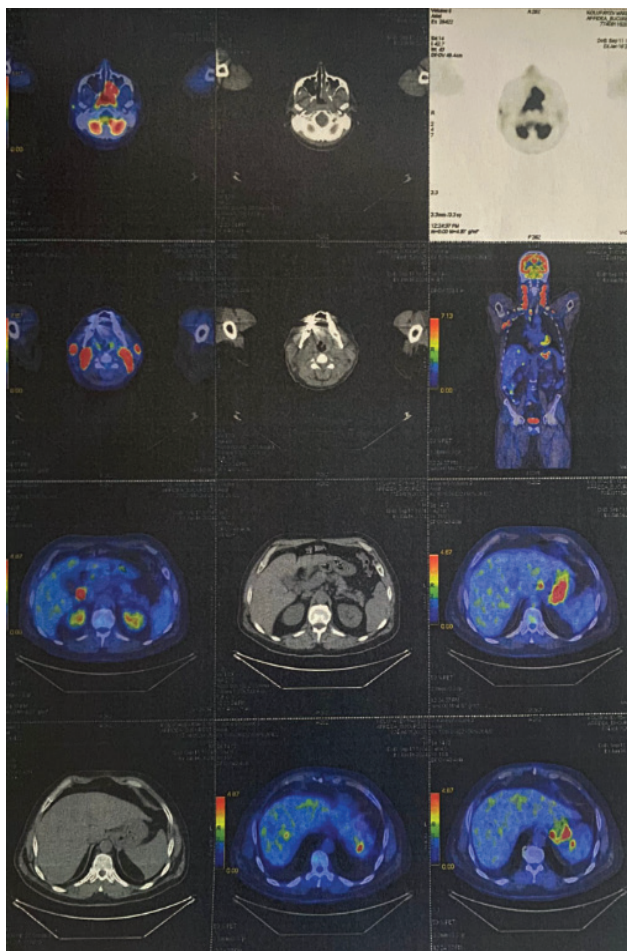


Figure 3: PET-CT with F18-FDG showing extensive nodal and extranodal hypermetabolic lesions, consistent with disseminated lymphoproliferative disease

Additional investigations were necessary before formulating a diagnosis. In order to establish the etiology, upper digestive endoscopy is performed, which shows multiple ulcer-infiltrative formations with raised edges that extend along the greater gastric curvature and at the level of the fornix - biopsies are taken. Histopathological examination: fragments with foveolar epithelium with regenerative changes, areas of ulceration and the presence of medium/small discohesive cells, with atypical nuclei, diffusely arranged in the lamina propria, with extension into the submucosa. Immunohistochemical examination: CK7 negative in proliferated cells, CD 20 + intense in tumor cells, CD 10 +, Cyclin D1 in very rare isolated tumor cells (below 2%), Bcl-2 variable nuclear position in approx. 50% of tumor cells, Ki67 predominantly intense nuclear position in approx. 85% of tumor cells.

Based on clinical symptoms, imaging

investigations and the result of the gastric biopsy, the patient was diagnosed with diffuse large B-cell gastric non-Hodgkin lymphoma GCB (germinal center B-cell phenotype/Hans algorithm).

Despite the institution of specific oncological treatment, the clinical evolution was rapidly progressive and unfavorable, with the patient's death.

Discussions

HIV-associated non-Hodgkin lymphomas continue to represent a major diagnostic and therapeutic challenge, even in the context of the widespread use of effective antiretroviral therapy. Although ART significantly reduces the incidence of AIDS-defining neoplasms, NHL remains one of the most common causes of morbidity and mortality in this category of patients (12,13,14).

The presented case illustrates the fulminant evolution of a diffuse large B-cell lymphoma of the GCB type in a patient with newly diagnosed HIV infection, on ART and with documented viro-immunological improvement. The increase in the number of CD4 lymphocytes and the suppression of the viral load were not sufficient to prevent the development of an aggressive hematological malignancy, a fact also reported in other studies in the literature (15,16,17,18). This aspect suggests that the oncological risk may persist even in conditions of apparently effective control of HIV infection.

The patient's clinical presentation, characterized by significant weight loss, epigastric pain, and generalized adenopathy, is typical of HIV-associated NHL, but the extensive extranodal involvement – gastric, hepatic, splenic, nasopharyngeal, and intestinal – indicates a high degree of tumor aggressiveness. Advanced imaging, especially PET-CT with F18-FDG, played an essential role in assessing the extent of the disease, highlighting the wide dissemination and intense metabolic activity of the lesions.

Large B-cell lymphoma of germinal centers was confirmed through histopathological and immunohistochemical diagnosis. This was characterized by a very high proliferation index (Ki-67 ~85%), a marker of poor prognosis. The intense expression of CD20 and CD10 supports

the biological aggressiveness of the tumor, and the extent of systemic involvement explains the rapidly progressive evolution observed in this case.

An important aspect to emphasize is the difficulty of the initial differential diagnosis in the context of HIV infection, where nonspecific symptoms can be attributed to opportunistic infections or other complications related to immunosuppression. This can lead to diagnostic delays, with a negative impact on the prognosis. Therefore, the appearance of systemic symptoms, progressive adenopathies or extranodal lesions in HIV patients should promptly raise the suspicion of a lymphoproliferative disorder.

The poor outcome, despite the rapid initiation of specific treatment, reflects the intrinsic aggressiveness of HIV-associated NHL and confirms the literature data showing increased mortality rates in these settings (19). Optimal management of these patients requires a multidisciplinary approach, involving specialists in infectious diseases, hematology, oncology, pathology and imaging, as well as careful monitoring of interactions between chemotherapy and ART.

In conclusion, this case highlights that HIV-associated non-Hodgkin lymphoma can have a rapid and lethal course, even in the context of an apparently favorable viro-immunological response. Clinical vigilance, early evaluation, and prompt therapeutic approach remain essential to improve survival in HIV patients who develop hematological malignancies.

Conflict of Interest

The authors report no conflict of interest in this work.

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