Undiagnosed HIV-related lymphoma associated to EBV co-infection: an autopsy case report

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Research Article

Keywords: HIV, Sudden death, Acute liver failure, Non-Hodgkin Lymphoma, Epstein-Barr virus, case report

Posted Date: April 29th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-425466/v1

Abstract

Background:

The diffuse large-B-cell lymphoma (DLBCL) is known as one of the most neoplasm that occurs in AIDS patients. In rare cases, this tumor is manifested with acute liver failure.

Case presentation:

We report a case of patient who was presented with jaundice and hepatomegaly due to an acute liver failure. A blood exposure accident helped the operator to discover the seropositive statue of the deceased. The results confirmed the presence of HIV antibodies in patient's serum. Macroscopic examination of the spleen showed a well-defined subcapsular nodule. It had a micronodular appearance. Immunohistochemistry was also performed.

Conclusion:

The diagnosis of DLBCL related to HIV associated to an Epstein-Barr infection was established in postmortem.

Background

Non Hodgkin lymphomas have been the most frequent neoplasm in AIDS patients [1]. The relation between the two diseases is certainly proved. Moreover, lymphoma diagnosis in AIDS patients can be established at autopsy also as it is reviewed in many cases [2]. The secondary involvement of the liver is frequent in the evolution of lymphoma related HIV and indicates an advanced stage [3]. Most of these patients are usually presented with non-specific symptoms and signs (jaundice, fever, hepatomegaly) in addition to abnormal liver function tests (cholestasis and cytolysis) [4]. There were sporadic case reports of acute liver failure due to non-Hodgkin lymphoma [5].

We report a case of an unusual discovering of DLCBL related to HIV associated to an Epstein Barr infection.

Case Presentation

An imprisoned 54-year-old man presented to the Emergency Department with five days-history of abdominal pain and fatigue. He had a history of diabetes, dyslipidemia and coronary heart disease that required three revascularization interventions. On examination there was jaundice and hepatomegaly. Biological analyses showed normal rates of the white blood cells, hemoglobin, platelet and prothrombin time. It also revealed an increased rate of creatinine (137umol/l), low serum albumin (26.9 g/l), cholestasis (bilirubin 189 IU/L; alkaline phosphatase 1093 IU/L; gamma glutamyl transpeptidase

774 IU/L) and cytolysis (serum aspartate aminotransferase 234 IU/L; serum alanine aminotransferase157 IU/L; lactate dehydrogenase 1257 IU/L).

The abdominal ultrasound demonstrated heterogeneous hepatomegaly and normal aspects of the spleen and the kidneys. The next day, the patient was admitted to the Gastro-Enterology Department. He presented also low glucose levels ranging from 0, 36 g/dL to 0, 73 g/dL despite that he did not take his anti-diabetic medication and was continuously perfused with glucose containing solution. A first diagnose of suicide attempt by oral anti-diabetic medication was suspected. Neurological and hemodynamic state were rapidly altered (low blood pressure with rapid and weak pulse, and a Glasgow score at 7/15). Blood analysis lactic acidosis with blood pH of 6.8, high rates of Potassium (7.5 mmol/L), creatinine (455 umol/L) and deterioration of biochemical parameters of the liver. The prothrombin time had increase to 40%. Electrocardiography was normal.

A conditioning and an urgent hemodialysis were performed with no improvement. The patient presented a cardio-respiratory arrest and died two days after admission with multiple organ dysfunction syndrome. No diagnosis was retained. A medico-legal autopsy was ordered by the coroner.

During autopsy, the resident examiner was accidentally injured with the scalpel blade. A viral serology panel of both the resident and the deceased was performed. The results confirmed the presence of HIV antibodies in patient's serum. Macroscopic examination of the spleen, which weighted 150 g, showed a well-defined subcapsular nodule, greyish, measuring 1.5 cm in diameter (Fig. 1a). The rest of the splenic parenchyma is free of gross lesions. The liver weighted 4085 g and measured 26x24cm. It had a micronodular appearance (Fig. 1b).

In histology, the different liver samples showed similar histological aspects. The liver tissue was unrecognizable due to the presence of necrosis and especially of an infiltration of this tissue by a proliferation made by large lymphoid cells, some of which are in apoptosis (Fig. 2a and 2b). The tumor located in the spleen demonstrated the same cells described in the liver.

Immunohistochemistry study showed that the tumor cells expressed in a diffuse and in intense way the CD20 (Fig. 2c) and Latent Membrane Protein-1 (LMP-1) (Fig. 2d). CD3 and CD5 were absent.

Conclusions

In this case, the patient developed an acute liver failure causing multiple organ dysfunction syndrome with undetermined etiology. Despite the absence of ante-mortem arguments for suspecting lymphoma, necropsy revealed the involvement of the liver and the spleen by a non-Hodgkin lymphoma related to an HIV infection. This infection was also discovered after a post-mortem blood exposure accident.

In industrialized countries, 19% of patients infected with AIDS were presented non-Hodgkin lymphoma. The diagnostic was retained within autopsy in 40% of cases [2]. The detection of visceral non-Hodgkin

lymphomas is rare and probably due to low life expectancy of the African patients with high rate of opportunistic infection and advanced HIV disease [6].

In the present report, the patient had no previous history of lymphoma and presented to the emergency room with acute liver failure. In fact, hematological malignancies such as non-Hodgkin lymphoma is exceptionally a cause of acute liver failure. The involvement of the liver in HIV patients with non-Hodgkin lymphoma is well known. According to literature this incidence varies between 16% and 22% in untreated patients [7, 8]. As in the reported case, patients with hepatic lymphomatous infiltration usually manifested with hepatomegaly and jaundice. However, an important number of these patients were asymptomatic and had normal liver function [9].

There were a few researches reporting acute liver failure during the course of non-Hodgkin lymphoma. According to a study concerning 18 patients presenting with acute liver failure secondary to malignant hepatic infiltration admitted to Liver Failure Unit at King's College Hospital over an 18-year period, the diagnosis of NHL was made in nine patients. Seventeen of them died due to multiorgan failure and there is only survivor. The diagnosis was in a postmortem examination in three cases [5, 10].

It is difficult to make the diagnosis of malignant liver infiltration in patients who presented with acute liver failure. It can be more difficult especially in the case of an unknown primary disease as is our case.

Another remarkable fact of this presented case is that the HIV infection were diagnosed at post mortem after a blood exposure accident. Indeed, the patient unknown statue as seropositive and the quick evolution of the disease may explain the initially-missed diagnosis.

The histological and the immunochemistry were of a great help. Diffuse large cell B lymphomas associated with immunosuppression and diagnosed in post-mortem are unusual. In the context of immunodeficiency, these lymphomas are generally, although not always, EBV+. In this report, LMP-1 was positive. In Western Europe and America, approximately 50–70% of HIV associated-DLCBL are EBV positive and express the transforming LMP-1. LMP-1 plays a critical role in the transformation of B lymphocytes [11]. This confirms the participation of EBV in the genesis of this tumor. Unfortunately, we did not perform an in-situ hybridization study due to technical and financial problems.

This case report shows the importance to include non-Hodgkin lymphoma on the list of causes of acute liver failure. The post-mortem examination highlighted the importance of the pathological characteristics of the Lymphoma.

Abbreviations

- DLCBL : diffuse large-B-cell lymphoma
- LMP-1 : latent Membrane Protein-1

Declarations

Ethics approval and consent to participate:

All procedures performed in this study (involving human) were in accordance with the ethical standards of the “Research Ethics Committee, Faculty of Medicine, University of Monastir, Tunisia” and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This research was approved by the above-mentioned Committee.

Consent for publication:

Informed and written consent for publication was obtained from the family of the deceased subject. There were no identifying images published in this study.

Availability of data and materials:

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests:

All authors declare that they have no financial or personal relationships with other people or organisations that could inappropriately influence their work.

Funding:

None.

Authors’ contribution statements:

All authors contributed to the study conception and design. Conceptualization and supervision were performed by NHS. Material preparation, data collection and analysis were performed by MG, SS, AB, SBJ and SBH. The first draft of the manuscript was written by MG and SS and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Acknowledgments:

We want to express our deepest gratitude to Mr Abdelaziz Zaoui, our autopsy room preparator, for the good work.

Authors’ information:

Not applicable.

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Figures

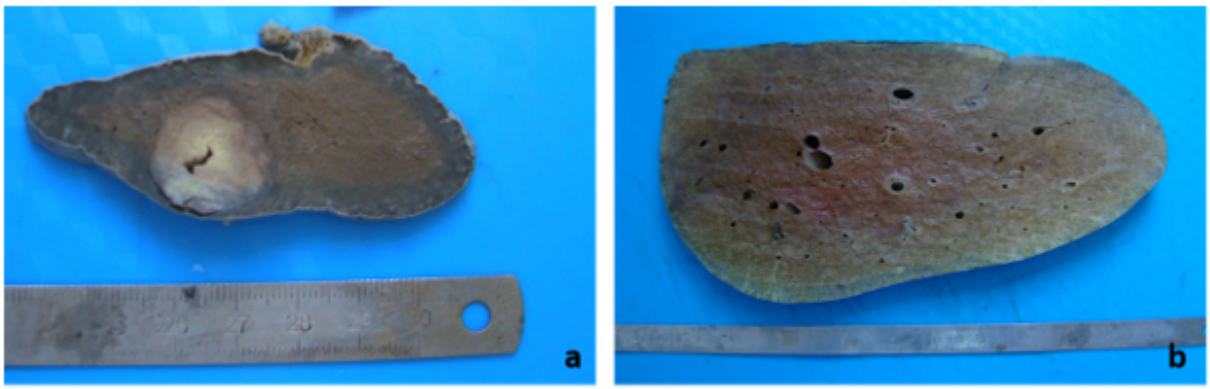

Figure 1

(a) Cut gross section of a subscapular spleen nodule. (b) Liver slice showing micronodular appearance.

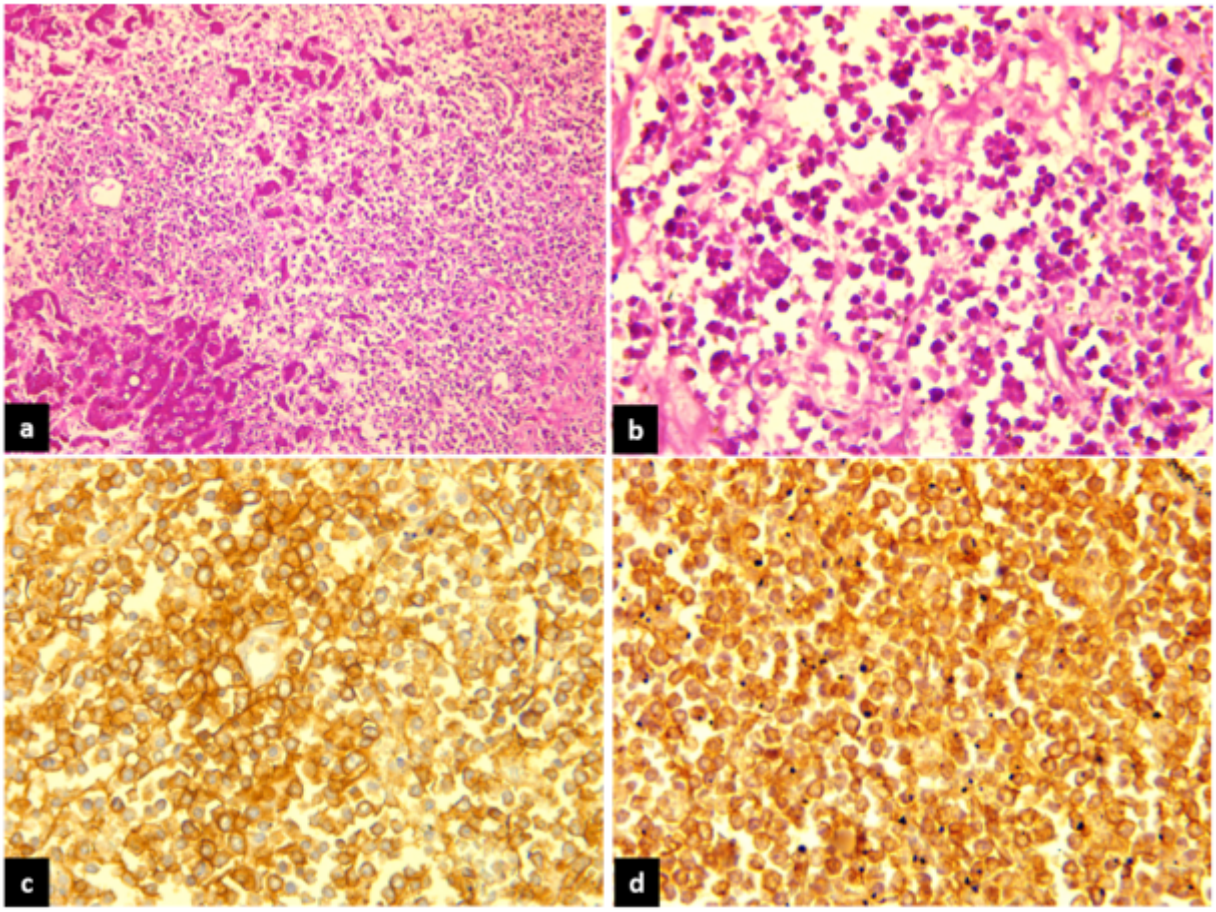

Figure 2

(a) Massive infiltration of liver tissue by lymphoid proliferation (HE x 100). (b) Lymphoid cells are large to medium-sized with atypical nucleus (HE x 400). On immunohistochemistry, tumor cells show diffuse and strong positivity of CD20 (c) and LMP1 (d) (HE x 400).

Supplementary Files

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