

Primary effusion lymphoma in women with acquired immunodeficiency syndrome (AIDS), pleural effusion, and ascites: cytological diagnosis and immunocytochemistry

Linfoma primário de efusão em mulher com síndrome da imunodeficiência adquirida (SIDA), derrame pleural e ascite: diagnóstico citológico e imunocitoquímico

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ABSTRACT

The primary effusion lymphoma is a rare type of non-Hodgkin form that manifests with cavity stroke, usually associated with immunosuppression. It is associated with infection with the human herpes virus 8 (HHV-8), a necessary fact to confirm the diagnosis. This report describes the primary effusion lymphoma, diagnosed by cytology and immunocytochemistry, in patients with the unusual manifestation of involvement of two serous cavities. Its prognosis is poor, and treatment is limited.

Key words: Non-Hodgkin Lymphoma; Pleural Effusion; Ascites; Herpesvirus 8, Human.

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RESUMO

O linfoma primário de efusão é tipo raro de forma não Hodgkin que se manifesta com derrame cavitário, em geral associado à imunodepressão. Associa-se à infecção pelo vírus herpes humano 8 (HHV-8), fato necessário para que seja confirmado seu diagnóstico. Este relato descreve o linfoma primário de efusão, diagnosticado por meio de citologia e imunocitoquímica, em paciente com manifestação não usual de comprometimento de duas cavidades serosas. Seu prognóstico é reservado e seu tratamento é limitado.

Palavras-chave: Linfoma não Hodgkin; Derrame Pleural; Ascite; Herpesvirus Humano 8.

INTRODUCTION

Primary effusion lymphoma, also known as primary cavity lymphoma, is a rare non-Hodgkin lymphoma of mature B lymphocytes with large cell morphology that is manifested by a cavity stroke, usually in a serous cavity.¹ Extracavitary masses should be absent but can occur in the pleura, gastrointestinal tract, skin, lungs, brain, and lymph nodes when in the advanced phase.² Most patients are young or middle-aged men with severe immunosuppression commonly caused by infection with the human immunodeficiency virus (HIV). It also affects immunocompromised patients due to liver cirrhosis and immunosuppressive therapy for organ transplant.³ In rare cases, it can affect immunocompetent patients, usually elderly. There is no well-defined treatment protocol, and the disease has a poor prognosis.

This report describes the primary lymphoma effusion, a rare lymphoid neoplasm, that is diagnosed through cytology and immunocytochemistry in patients

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with an unusual manifestation of involvement of two serous cavities (pleural stroke and ascites) associated with HIV infection and acquired immunodeficiency syndrome (AIDS).

CASE REPORT

Female patient, 42 years old, HIV seropositive, diagnosed two years ago and who developed abdominal pain and cough a week ago. She was in a good general condition, with tachycardia, tachypnea, normotensive, and abdominal bloating due to mid-volume ascites confirmed by abdominal ultrasound and pleural stroke by chest X-ray. The thoracic and paracentesis assessment generated clinical specimens for laboratory evaluation. The cytological examination of pleural and ascites fluids showed a sediment rich in large lymphoid cells, round, non-attached, with high nucleus-cytoplasm ratio, hyperchromatic nuclei, pleomorphic, with prominent nucleoli and small cytoplasm, basophilic and microvacuolized, and numerous cells with karyorrhexis (Figure 1).

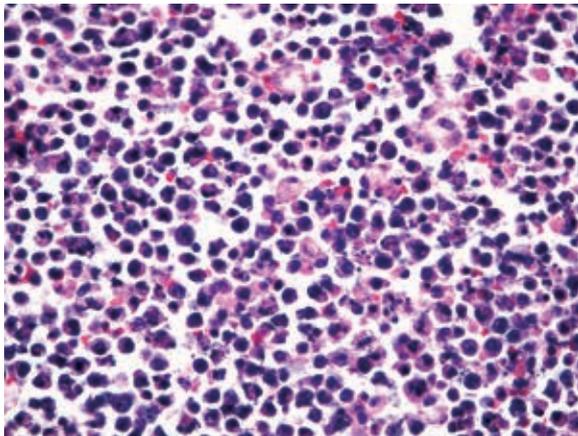


Figure 1 - Cytological examination of ascetic fluid showing neoplastic lymphoid cells, HE (40X).

The immunocytochemistry study showed neoplastic cells positive for CD45, HHV-8, (Figure 2), and vimentin and a cell proliferation rate of 80% evidenced by the Ki-67 marker. The negativity of cells to CD3, CD20, AE1/AE3, Melan-A, and S-100 was observed. The diagnosis was established as primary effusion lymphoma. A few days after diagnosis, the patient died of respiratory failure.

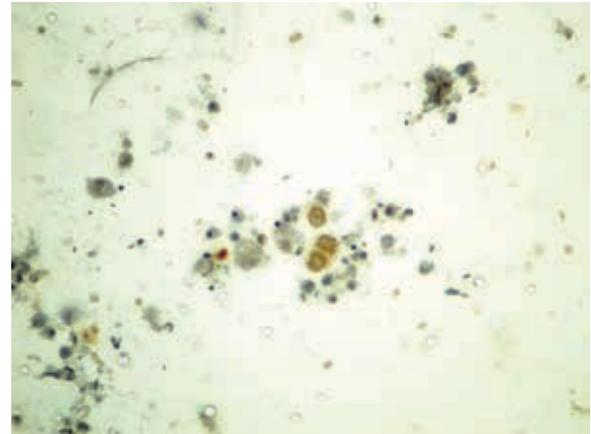


Figure 2 - Neoplastic cells positive for HHV-8 in the immunocytochemical examination (40X).

DISCUSSION

Cavity strokes have various causes in HIV-positive patients⁴ and constitute a clinical diagnostic challenge.⁵ Cytology is an integrated part of the evaluation algorithm of aspirated fluid for a differential diagnosis between dozens of functional, inflammatory, infectious, and neoplastic conditions.⁶

The primary effusion lymphoma is a rare tumor neoplasia that manifests with cavity strokes, especially with immunosuppression and ascites, and pleural and pericardial stroke.

The immunosuppression is a comorbidity associated with primary effusion lymphoma, and even to its presence as a rare complication for the treatment of intestinal inflammatory disease.⁷ Moreover, there is the possibility that hypogammaglobulinemia may contribute to its development.⁸

It is associated with the infection by the human herpes virus 8 (HHV-8) as a prerequisite for its diagnosis. The HHV-8 infection, common in other diseases such as Kaposi's sarcoma and Multicentric Castleman's disease,^{9,10} is not well-controlled *in vivo*, probably because of a failure to recognize the infected cells and cytotoxicity caused by T lymphocytes¹¹, which allows a latent infection in the body. The HHV8 acts in the pathogenesis of cancer by coding genes that confer proliferative and antiapoptotic signals. Co-infection with the Epstein-Barr virus (EBV) is also common; however, without pathogenesis influence.¹² It is associated with HIV infection in 90 to 95% of cases and EBV in most cases. However, EBV negative cases are observed in general in the elderly from the Mediterranean region.^{12,13}

Material from cavity effusion aspirates immersed in paraffin is useful to carry out additional studies such as immunocytochemistry and *in situ* hybridization.¹⁴ Cells from primary effusion lymphomas are atypical lymphocytes, large, commonly pleomorphic, and possibly anaplastic and positive for the CD45 marker and negative for B and T lymphocyte lineage markers. Positivity for lymphocyte activation markers (CD30, CD38, CD71, and epithelial membrane antigen) is generally observed in addition to plasma cell differentiation (CD138) and B lymphocyte late stage differentiation (MUM1).¹⁵

The definitive diagnosis is achieved by detecting the infection with HHV-8 in tumor cells based on the nuclear antigen expression associated with the latency (LANA-1) revealed by immunocytochemistry¹⁶ and clonal rearrangements of immunoglobulin genes in molecular studies that indicate the origin in the B lymphocyte post-germinal center.

There are cases of solid positive cavity lymphomas without stroke and positive for HHV-8. Despite the small clinical and immunohistochemical differences in these lymphomas, profile studies of gene expression and proteomic analysis indicate that they belong to the effusion primary lymphoma spectrum.¹⁷ The formation of ascites and emergence of single or multiple solid tumors in different organs and tissues of the cavity abdominal are observed in mice animal models with immunodeficiency in which HHV-8 positive lymphomatous cells are injected into the peritoneal cavity.¹⁸

The primary effusion lymphoma is a neoplasia with a high mortality rate in most cases after one year of diagnosis. Advanced age limits the use of chemotherapeutic agents, providing relapse and loss of effusion control.¹⁹ In immunocompromised patients and those treated for HIV with highly active antiretroviral therapy, the use of chemotherapy is limited by the sum of the immunosuppression deleterious systemic effects and others from this therapy.

The prognosis of primary effusion lymphoma is reserved, and its treatment is little effective. The therapy with second-generation lenalidomide immunomodulator has been tested with better results and tolerability and no side effect.²⁰ There is also the pleurodesis therapy with bleomycin when it is limited to the pleural cavity.²¹

CONCLUSION

The diagnosis and clinical evolution of primary effusion lymphoma are described, which manifests

itself with double cavity strokes without clinical suspicion, defined in pleural and ascites liquid aspirates embedded in paraffin and used in the immunocytochemistry analysis.

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