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CASE REPORT

An Unusual Case of Posttransplant Peritoneal Primary Effusion Lymphoma with T-cell Phenotype in a HIV-negative Female, not Associated with HHV-8

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Primary effusion lymphoma (PEL) is a recently individualized form of non-Hodgkin's lymphoma (WHO classification) that mainly develops in HIV infected males, more frequently in homosexuals and advanced stages of the disease (total CD4+ lymphocyte count below 100-200/μL). Occasionally, it appears in other immunodepressive states (such as solid organs transplant period) and even, although very rarely, in immunocompetent patients. From a pathogenetic point of view, PEL has been related to Kaposi's sarcoma associated herpes virus (also named human herpesvirus 8, HHV-8), an etiological factor of Kaposi's sarcoma. The relative infrequency of this disease, the absence of wide casuistics allowing a better characterization, and its unfavorable outcome support the need of a deeper knowledge. We present here the clinical-biological findings of a patient, HIV-seronegative, who was diagnosed with peritoneal PEL of T-cell origin, and not HHV-8-associated, five years after renal transplantation. (Pathology Oncology Research Vol 11, No 3, 178–181)

Key words: primary effusion lymphoma, non-Hodgkin's lymphoma, immunohistochemistry

Introduction

Primary effusion lymphoma (PEL) has been recently identified as a distinct subtype of non-Hodgkin's lymphoma associated with infection of the neoplastic lymphoid cells by the Kaposi's sarcoma-associated herpesvirus/human herpesvirus 8 (HHV-8).[1,2] Primary effusion lymphoma has characteristic clinicopathologic features, including initial presentation as a lymphomatous effusion usually in the absence of a detectable tumor mass, occurs mostly in human immunodeficiency virus (HIV)-positive men, and has a morphologic structure that bridges large cell immunoblastic and anaplastic large cell lymphoma (ALCL).[1,2] Neoplastic lymphoid cells are B cells with a peculiar phenotype. They usually lack surface immunoglobulin and B-cell-associated antigens such as CD19 and CD20, and express CD45, CD30, and antigens associated with late stages of B-cell differentiation such as CD138.[1,2] Genotypic analysis of PEL has revealed clonal immunoglobulin gene rearrangements in all cases.[1,2] We describe here a unique case among PELs arising in a HIV-seronegative female, not associated with HHV-8 infection, after renal transplantation.

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Case report

We report a case of a 27-year-old woman who was admitted to our hospital because of dizziness, headache and malaise. Five years earlier the patient had a renal transplantation due to chronic renal failure. From that period the patient was under immunosuppression. She was HIV-negative. On physical examination ascites was found but no peripheral lymphadenopathy or hepatosplenomegaly. Laboratory data on admission was as follows: WBC=6.7x10^3/μl, hemoglobin=12.5 g/dl, platelets= 409x10^3/μl, LDH=144 U/I, total protein=3 g/dl, albumin=1.2 g/dl, cholesterol=217

mg/dl, liver function tests, amylase and lipase were normal. HIV screen was negative. Peritoneal fluid showed albumin <1 g/dl, LDH=27 U/I, WBC=1/µl. Because all blood tests and CT scans of the abdomen and chest could not interpret the patient's symptoms, an exploratory laparotomy was performed. During the operation, 3 l ascitic fluid were removed, but no other abnormalities were found except from a slightly thickened omentum and peritoneum from which biopsy samples were obtained. Cytological examination of the fluid, histologic interpretation of the excised specimens, immunophenotypic and molecular workup was indicative of primary T-cell effusion lymphoma. The patient received chemotherapy with endoxan, farmorubicin, oncovin and prezolon, but three weeks later died due to postoperative complications.

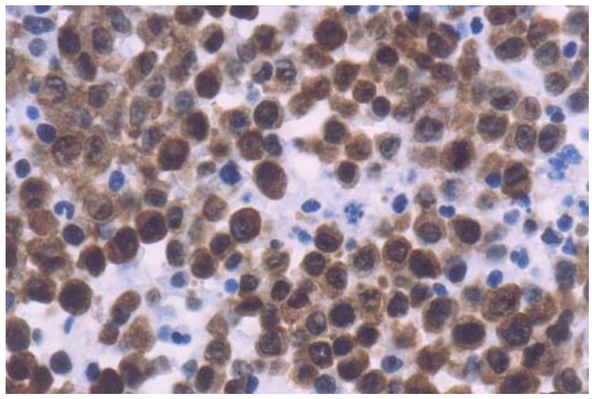

Figure 1. *Discohesive, large, pleomorphic cells, among a small number of small lymphocytes in the background. Direct smear from the ascitic fluid, Papanicolaou stain, x400.*

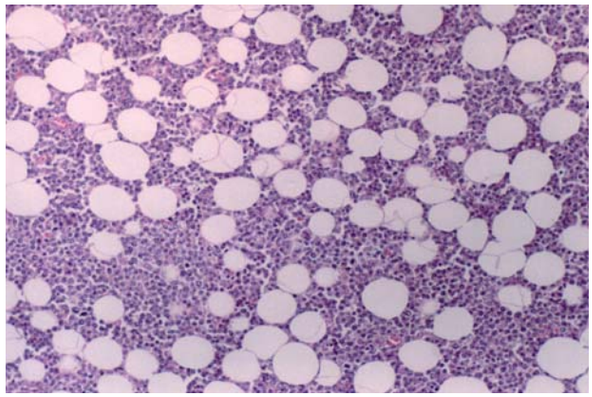

Figure 2. *Diffuse infiltration of fatty tissue by large lymphoid cells, HE stain, x100*

Materials and methods

Cytological, histological and immunophenotypic studies

Direct smears from the peritoneal effusion were stained with Papanicolaou. Tissue samples from the peritoneum and the omentum with maximum diameter of 18 cm and 1 cm, respectively, were routinely processed for histologic examination.

Immunophenotyping was performed on tissue samples from the peritoneum and omentum. The alkaline phosphatase anti-alkaline method (Dako, Glostrup, Denmark) was used with antibodies against human cytokeratin KL1 and MNF116, EMA, CD45, CD2, CD3, CD5, CD19, CD20, CD79a, CD138 (Syndecan-1), and CD30 antigens; anaplastic lymphoma kinase (ALK1) protein; EBV latent membrane protein 1; and TIA-1. All antibodies were purchased from Dako, except AKL1 (Immunotech, Marseille, France), CD138 (clone B-B4; Serotec, Oxford, England), and TIA-1 (Coulter, Marseille, France). Flow cytometry, a more desirable means of determining immunophenotype in suspected lymphomas, was not performed because of the scarcity of the specimens.

Molecular analyses

DNA was extracted from tissue samples. T-cell receptor γ chain analysis was performed by polymerase chain reaction (PCR) as described.[3] The presence of EBV was tested by PCR using EBER primers, and p53 exon 6 primers were used to confirm the integrity of the DNA and the lack of PCR inhibitors.[4,5] The presence of KSHV sequences was examined by PCR using primers KS330233F and KS330233R, which amplify a 233-bp fragment as previously reported.[6]

Results

Direct smears from the ascitic fluid (*Figure 1*) showed noncohesive, large to very large size lymphoid cells with abundant basophilic cytoplasm. The cells exhibited features that appeared to bridge large-cell immunoblastic and anaplastic large cell lymphoma. They contained large, pleomorphic, round to multilobated or kidney-shaped nuclei that often disclosed prominent nucleoli. A few cells showed eccentric nuclei, surrounded by a prominent clear perinuclear Golgi zone. Mitotic figures were abundant. Apoptotic neoplastic cells were noted. Histology revealed a diffuse infiltration of the fatty tissue (*Figure 2*) by large lymphoid cells with abnormal nucleus, 1 to 2 prominent nucleoli and amphophilic cytoplasm. Mitotic figures were numerous. Immunohistochemically tumor cells were negative for cytokeratin (KL1, MNF116) and EMA.

Most neoplastic lymphoid cells were strongly positive for CD30 (*Figure 3*), CD8, and CD3 (*Figure 4*), and showed weak staining for CD45, whereas they were negative for CD19, CD20, and CD79a. Syndecan (CD138) was also absent except on a few mature plasma cells. Tumor cells did not express CD2, CD5, TIA1, or ALK1. PCR analysis of T-cell receptor γ chain gene rearrangement showed the presence of a predominant T-cell clone

within an oligoclonal T-cell expansion. No clonal rearrangement of IgH chain gene was found. The search for EBV infection was negative both by immunohistochemistry and PCR analysis. No HHV-8 DNA sequences were detected by PCR either. The patient's serum did not contain anti-HHV-8 antibodies. Finally, the diagnosis of primary effusion lymphoma with T-cell immunophenotype was established.

Discussion

PEL selectively involves the serous body cavities, occurs predominantly in immunodeficient patients and is frequently infected by human herpesvirus type 8 and Epstein-Barr virus. Severe immunosuppression promotes the emergence of lymphoproliferative disorders in patients undergoing solid organ transplantation. As with other high-grade lymphomas, prognosis is very poor with median survival of only a few months. Death is usually due to lymphoma. The immunophenotype is also extremely unusual because the lymphoma was of T-cell lineage.

In patients with ascites, especially in the setting of immunosuppression, PEL should be suspected in the absence of a suspicious mass.

Oshima et al[7] have suggested that multistep genomic abnormalities might be involved in HHV-8/HIV-negative PEL tumorigenesis. Shimazaki et al[8] have presented an unusual case of PEL; a subset of Burkitt-like disease, although classified as large cell lymphoma, because of B-cell phenotype and c-myc gene rearrangement.

In the present case, phenotypic and genotypic findings disclosed the T-cell origin of lymphoma cells. Indeed, neoplastic cells were negative for CD19, CD20, CD79a, CD138, and did not exhibit clonal IgH rearrangement by PCR analysis. By contrast, they strongly expressed CD3, and a clonal rearrangement of T-cell receptor γ chain gene was found. Primary effusion lymphoma exhibiting a T-cell phenotype was reported only once, in an HIV-seropositive male patient.[9] In the latter case, neoplastic lymphoid cells expressed various T-cell-specific antigens, including CD2, CD3, CD5 and CD7, and no B-cell markers, and both T-cell receptor and immunoglobulin gene rearrangements.[9] In our case, several features could be suggestive of ALCL. However, ALCLs commonly present with systemic disease, and isolated peritoneal effusion is uncommon. In addition, ALCLs are usually associated with a t(2;5)(p23;q35) translocation that leads to an abnormal expression of ALK, a feature that was not observed in our case.[10] Moreover, TIA1, a cytotoxic marker frequently detected in ALCL was not present.[10]

With a presentation as a peritoneal effusion and pleomorphic lymphoma cells identified in the fluid, the main diagnoses are anaplastic large cell lymphoma (ALCL) and PEL. A distinction between them is important because of the much better prognosis of the former. Similarities between ALCL and PEL may include similar morphologic features, CD30 expression, and apparently a null-cell immunophenotype.[11]

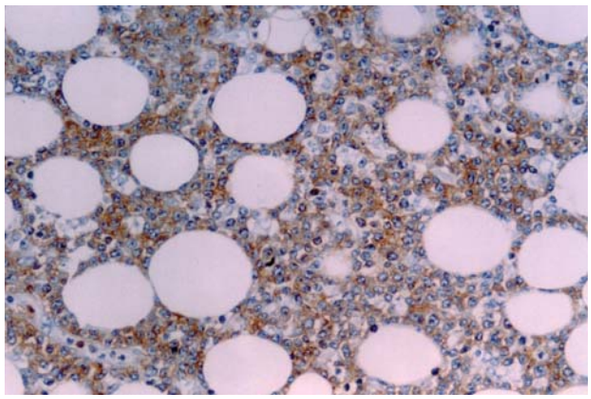

Figure 3. *Positive staining of lymphoma cells for CD30. Tissue section, immunostain, x200*

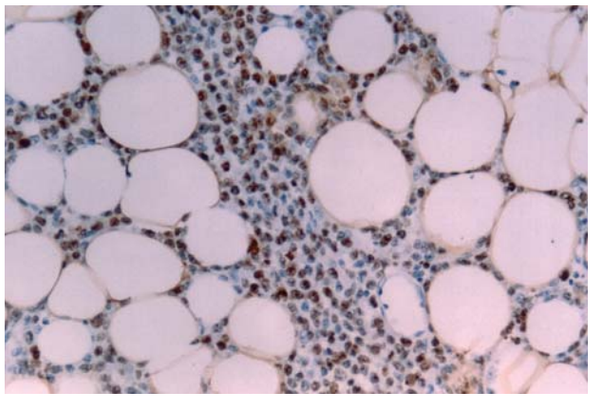

Figure 4. *Positive staining of lymphoma cells for CD3. Tissue section, immunostain, x200*

Features that favor PEL include known HIV infection, CD138 and MUM1 expression, and positivity for HHV-8 and EBV.11 Demonstration of a T-cell phenotype, absence of HHV-8 and EBV from the tumor cells and ALK expression would favor an ALCL.[11]

Our case highlights the importance of a multimodality approach in the workup of a lymphomatous effusion in arriving at a definite diagnosis. This case has been considered as a PEL in a HIV-, HHV-8-, EBV-negative patient, on the basis of its sharing some clinicopathologic features with this entity, like post-transplant history, initial presentation as a lymphomatous effusion without any detectable tumor mass and morphology that bridged peripheral T-cell lymphoma and anaplastic large cell lymphoma (CD3+, CD8+, CD30+).

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