

Diffuse large B-cell lymphoma arising from a multicentric mixed variant of Castleman's disease

Venizelos I, Tamiolakis D¹, Simopoulos C², Nikolaidou S¹, Barbagadaki S¹, Lambropoulou M³, Alexiadis G³, Boglou P³, Papadopoulos N³

Department of Pathology, Ippokration Hospital of Salonica, ¹Department of Cytology, General Hospital of Chania, ²Department of Experimental Surgery, Democritus University of Thrace, ³Department of Histology - Embryology, Democritus University of Thrace, Greece.

Abstract

This case report describes a patient with multicentric mixed type Castleman's disease and concomitant non-Hodgkin's lymphoma of diffuse large B cell type in the neck. Multicentric CD is a systemic illness with disseminated lymphadenopathy; its aggressive and usually fatal course is associated with infectious complications and risk for malignant tumors, such as lymphoma or Kaposi sarcoma.

Key Words: Castleman's disease; Non-Hodgkin lymphoma

Multicentric CD is a systemic illness with disseminated lymphadenopathy; its aggressive and usually fatal course is associated with infectious complications¹⁻³ and risk for malignant tumors, such as lymphoma or Kaposi sarcoma.^{4,7}

Case Report

A male aged 73 was admitted to our hospital for the first time with the complaint of fever and weakness, which had appeared 15 days previously. On clinical examination there was splenomegaly and bilateral cervical and axillary lymphadenopathy. Laboratory findings were significant: hemolytic anemia (hemoglobin level 6.3 g/dl, direct Coombs' test positive), hypocalcemia and polyclonal hypergammaglobulinemia. Immunophenotypic peripheral blood profile was consistent with viral infection (CD3: 40%, CD8: 18%, CD4: 22%, NK: 40%). Bone marrow aspirate and trephine examination showed a normal cell population. Imaging studies, including standard posteroanterior and lateral chest X-ray, abdominal X-ray, whole body computed tomography, and ultrasonography showed evidence of

supraclavicular and axillary lymphadenopathy and splenomegaly. Contrast-enhanced CT of the thorax (after bolus injection of contrast medium) showed no contrast enhancement in supraclavicular and axillary lymphadenopathy. Serological data were positive for anti-Coxsackie IgM antibodies. Immunologic studies were normal. Fine-needle aspiration biopsy (FNAB) was indicative of reactive lymphadenopathy. At excisional cervical lymph-node biopsy a diagnosis of Castleman's disease with features of both the hyaline-vascular and plasma-cell variants was established. The patient responded to corticosteroids (prednisone) but 4 months later he was readmitted with edema of the lower extremities, fever and weakness, hemolytic anemia, splenomegaly, remarkable lymphadenopathy of the chest and retroperitoneum, hypocalcemia, renal failure and noticeable peripheral blood profile: CD38: 100%, CD3: 78%, CD8: 56%, CD4: 22%, NK: 8%. A new excisional biopsy of a cervical node was performed and the result was diagnostic of malignant diffuse large B-cell lymphoma. Serology was negative for Kaposi sarcoma-associated herpesvirus KSHV/HHV8 and HIV, while the levels of serum C reactive protein, IL-6 and IL-10 were normal as well. The patient was treated

with CHOP, and passed away 6 months after the diagnosis of lymphoma due to complication with pneumonia and sepsis. No autopsy study was performed.

The gross examination of the first cervical lymph node biopsy specimen showed a fairly well-encapsulated, soft tan lesion with a largest dimension of 2.5 cm. Light microscopy, revealed areas of hyaline-vascular CD pattern, in which the majority of the lymphoid follicles had atrophic or regressive germinal centers often penetrated by capillaries. There was concentric layering of lymphocytes in an onion-skin appearance and one or more penetrating blood vessels. The interfollicular stroma was also prominent with numerous hyperplastic vessels of the postcapillary venule type and plump endothelial lining. In other areas a plasma cell CD pattern was seen with the characteristic monotonous sheets of mature-appearing plasma cells expanding into the interfollicular zones of the node. The follicular centers were enlarged and hyperplastic, in contrast to the atrophic follicular centers of the hyaline-vascular type. Although most of the plasma cells had abundant cytoplasm and small eccentric nuclei, occasional atypical forms with enlarged nuclei, irregular nuclear contours and prominent nucleoli were found. Immunohistochemical study in paraffin sections demonstrated, enlarged follicular dendritic cells (CD21+), decreased follicular center cell proliferation (CD20+, CD10+, CD5-, and negative for surface immunoglobulins), and an aberrant population of mantle zone lymphocytes (CD20+, CD10- and CD5-). The plasma cell infiltrates in the interfollicular areas were polyclonal by immunoglobulin light chain staining (positive for both κ and λ light chains). The

immunohistochemical staining for Bcl-2 oncoprotein was not expressed in follicular centers of the lymph node. Small T-lymphocytes and macrophages were detected in the follicular germinal centers by immunostaining with antibody to CD45RO and CD68 respectively.

These findings corresponded to Castleman's disease of mixed (transitional) variant (Figure 1).

Grossly, the node was enlarged (diameter 3 cm) with a diffuse yellowish color on the cut surface. At low magnification, the normal nodal architecture was totally effaced and the node was diffusely infiltrated by a population of atypical lymphocytes (large cleaved cells, large noncleaved cells, immunoblasts, multilobated cells, and anaplastic cells). Clusters of similar pleomorphic cells were additionally seen in perivascular areas and in sinuses, while proliferation of high endothelial venules was highlighted. Extensive infiltration of the lymph node capsule and surrounding fat was observed as well.

Slides were stained with CD45, CD79a, CD20, CD5, CD43, CD23, CD10, CD21, MIB-1, BCL-2, BCL-6 and p53, and polyclonal antibodies were used to determine the expression of CD3 antigen and of the Ig chains κ , λ , μ , γ , and α . The number of MIB-1 positive cells was determined by counting the number of cells with clear nuclear positivity per 100 cells in five high-power fields (X40 objective; BX40-Olympus). Immunostaining was carried using appropriate positive and negative controls.

The tumor cells were positive for CD20 (Figure 2), CD79a, CD45, CD10, BCL-2, and BCL-6, with

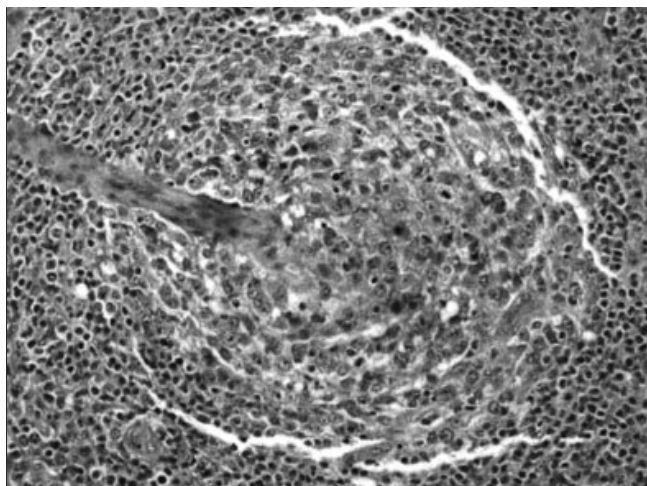


Figure 1: Hyaline-vascular changes, and solid, confluent sheets of plasma cells. Cervical node. Multicentric Castleman's disease of mixed type (H & E stain X100).

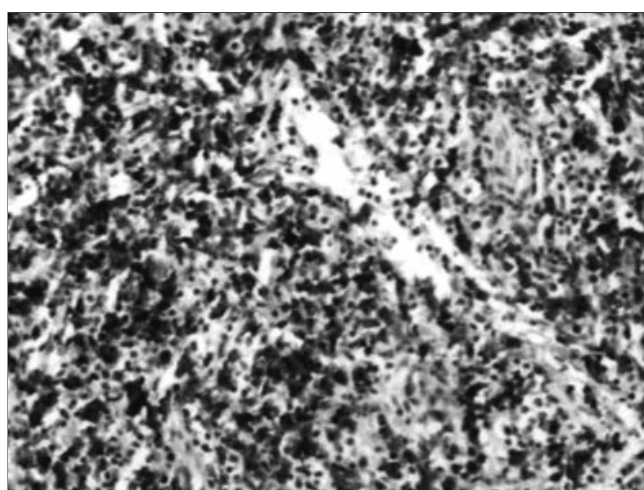


Figure 2: Pleomorphic lymphoid cells. Cervical node. Diffuse large B cell lymphoma (CD20 immunostain, X200).

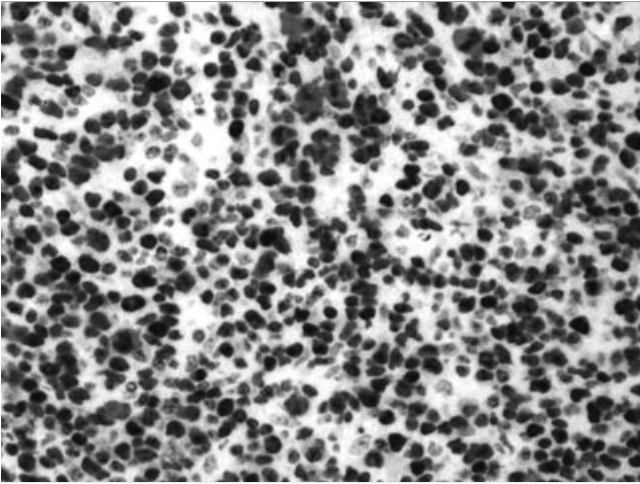


Figure 3: MIB-1/Ki67 positive lymphoid neoplastic cells. Cervical node. Diffuse large B cell lymphoma (Immunostain, X200).

absence of staining for CD3, CD5, and CD23. A monotypic expression of the light chain κ and of the heavy chain IgM was observed. Determination of the growth fraction revealed a large number of MIB-1/Ki67-positive cells comprising up to 80% of the neoplastic population (Figure 3). Molecular analysis showed a Bcl-2 oncogene rearrangement with t(14;18) chromosome translocation, and Bcl-6 oncogene rearrangement with translocation involving chromosome 3(3q27). EBV *in situ* hybridization was negative. The histological feature, and the immunohistological findings, led us to diagnose a diffuse large B cell lymphoma, according to the REAL/WHO lymphoma classifications.⁸⁻⁹

Discussion

In this case report, we describe a patient with a

combination of mixed type Castleman's disease and diffuse B-cell lymphoma arising in the neck. The most striking points in this case are: 1) the absence of malignancy in the first lymph node biopsy as had been demonstrated using the immunohistochemical analyses, 2) the fast evolution of CD to NHL (within 4 months) and 3) the negative serological test for HHV-8 and HIV; the positivity for the last one could explain the fast evolution.

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