



Anaplastic large cell lymphoma

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ABSTRACT

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Anaplastic large cell lymphoma is defined by a proliferation of large pleomorphic blasts and a constant expression of the CD30 molecule on all neoplastic cells, and has been clinically subdivided into a primary form and a secondary form. We are presenting a case of 14-year-old boy with reddish-livid papules on the skin of right half of trunk that were confluent in the lower end into solid plaque with diameter 20 x 15 cm, and enlarged lymph nodes in axilla and on neck. Lesioned skin biopsy, biopsy of lymph node and bone marrow showed pleomorphic cells, strongly CD30, and ALK positive. In our patient diagnosis was reached on the basis of morphological and immunohistochemical characteristics.

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KEY WORDS: Lymphoma, Large Cell; Cytodiagnosis; Immunohistochemistry; Child

INTRODUCTION

Anaplastic large cell lymphoma (ALCL) represents a generally recognized group of large cell lymphomas. ALCL was described for the first time in 1985 (1). Because of the sinusoidal localization and its lobular appearance this disease had earlier been interpreted as a variant of the malignant histiocytosis. ALCL is defined by a proliferation of large pleomorphic blasts and a constant expression of the CD30 molecule on all neoplastic cells.

Despite common expression of CD30 molecules, heterogeneity exists in the cytology and in the antigen profile of the tumor cells, and in the clinical features of patients affected by this condition. This has led to the distinction of several morphologic, immunophenotypic, and clinical subforms of ALCL. ALCL has been clinically subdivided into a primary form (*de novo*) and a secondary form (anaplastic transformation from another lymphoma). Among the primary ALCLs, systemic and cutaneous categories have been recognized both in immunocompetent patients and in HIV-positive patients (rarely). According to expression of ALK molecule, ALCL can be distinguished to anaplastic lymphoma kinase positive (ALK⁺) and anaplastic lymphoma kinase negative (ALK⁻) ALCL.

Diagnosis was reached using immunophenotyping of the skin biopsy and biopsy of the lymph node with the following antibodies: epithelial membrane antigen (EMA), CD34, CD79 α , CD20, CD3, CD15, CD5, CD7, CD45RO, CD30, and ALK-1.

CASE REPORT

We present a 14-year-old boy treated at the Clinic for Dermatovenerology in Niš. One month before admission to our Clinic, lymph nodes in his right axilla began to enlarge. Nodes were painful and mobile. Patient was examined by an oncologist in Pirot, and lymphadenopathy was diagnosed and antibiotic therapy was prescribed. Ultrasound of right axilla revealed several enlarged lymph nodes from 15 mm to 30 mm.

After few days, red, pruritic nodes appeared on the right side of trunk spreading toward right axilla. Patient had high temperature (39-40°C). Dermatologist was consulted, who diagnosed herpes zoster and started therapy with acyclovir. In short time, lymph nodes on neck started to enlarge too, and patient was sent to the Clinic for Dermatovenerology in Niš.

Patient has had vermicelli and mumps in childhood, otherwise was healthy. On admission, reddish-livid papules diameter 0.5 cm to 1 cm were seen on the skin of the right half of trunk that were confluent in the lower end into solid plaque with diameter 20 x 15 cm (Figure 1). In right axilla and on the neck lymph nodes were firm and painful to palpation.



Figure 1. Close-up view of lesions on trunk

During hospitalization patient had high temperature. Pediatrician-hematologist was consulted several times, who prescribed vancomycin, systemic ketokonazol, antipyretics, and analgesics.

The peripheral blood count was as follows: sedimentation 22/h, white blood cells (WBC) $6.7 \times 10^9/l$, red blood cells (RBC) $4.27 \times 10^{12}/l$, lymphocytes $1.5 \times 10^9/l$, monocytes $0.7 \times 10^9/l$, platelets $165 \times 10^9/l$, hemoglobin (Hb) 126 g/l, hematocrit (Hct) 38%, MCV 89 fL, MCH 29.5 pg, MCHC 332 g/l. Lactate dehydrogenase activity significantly increased (989.7 UL^{-1}). Serum glycemia, urea, and creatinine levels were normal. Aminotransferase activities were as follows: AST1 - increased activity (49.2 UL^{-1}), activity of ALP1 was normal (36.5 UL^{-1}), γ GT activity, and serum protein levels were normal. Serum albumin level was 50.4 gL^{-1} . Serum triglycerides level was normal, and cholesterol level was 3.22 mmolL^{-1} . Direct and indirect Coombs test remained negative. A complete work-up for infection including hemo-

culture, human immunodeficiency serology, Epstein-Barr virus, cytomegalovirus, and hepatitis B and C viruses was negative. Abdominal ultrasound showed normal liver and spleen, and no enlarged lymph nodes

Lesioned skin biopsy showed diffuse, dense, infiltrate of non-homogenous lymphocytes in subpapillary dermis, rare histiocytes and large bigger lymphocytes were present (Figure 2).

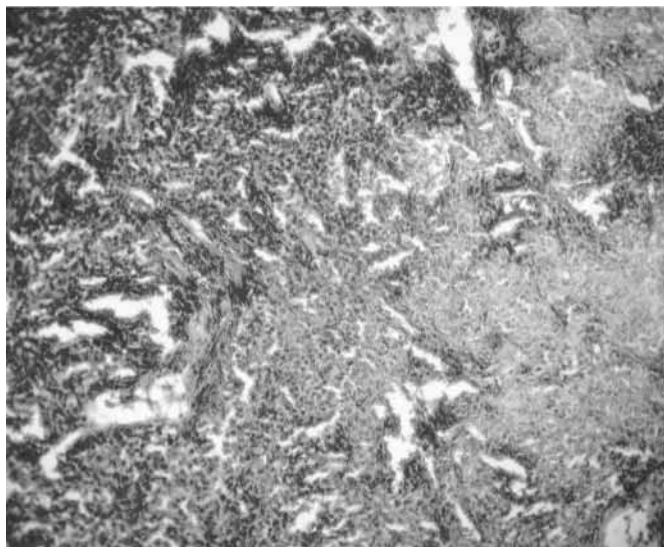


Figure 2. Skin biopsy, HE staining, nonepidermotropic infiltrate of tumor cells

Infiltration with same characteristics was shown around blood vessels. Immunophenotype of the cells were CD30 +++ and ALK-1 +++.

Biopsy of lymph node revealed sinusoidal system almost completely filled with pleomorphic cells, with large nuclei, prominent nucleoli and abundant cytoplasm. Mitotic and apoptotic indexes were high. The immunohistochemical studies demonstrated in all cells of tumor: EMA+ (membranous and in Golgi complex), CD34-, HLA-DR+, CD79 α -, CD20-, CD3-, CD15-, CD5+, CD7+, CD45RO+/-, CD30+++ , ALK-1+++ (Figure 3).

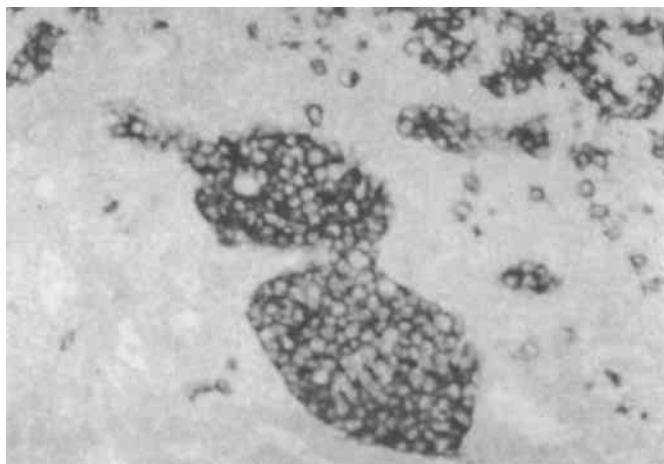


Figure 3. Biopsy of lymph node - APAAP, CD30 positive cells

Bone-marrow biopsy showed that nodular infiltrate consisted of large, multinuclear, anaplastic cells. Immunophenotyping showed CD30+++ and ALK-1+++.

DISCUSSION

ALK⁺ ALCL mostly occurs in the second and third decades of life with male/female ratio 6.5 (2). This lymphoma frequently presents as an aggressive stage III to IV disease, usually associated with systemic symptoms (75%), especially high fever that is same as in our case. Skin changes are often described. According to one study, skin involvement was

21%, bone 17%, soft tissues 17%, lung 11% and liver 8%, with a rare involvement of central nervous system and gut (3).

In our patient diagnosis was reached on the basis of morphologic and immunohistochemical characteristics.

Cells of ALCL are with large, often lobulated (horseshoe-shaped) nuclei (4). Nucleoli are present, often basophile. Cytoplasm is abundant, with clear cytoplasmic borders. The immunohistochemical studies demonstrated that most of infiltrated large cells are CD30 positive and usually CD3 negative (5). Prominent Golgy complex of neoplastic cells is intensively marked with CD30 and EMA antigens (6,7). In our case, morphologic and immunohistochemical features of neoplastic cells were as described. Large anaplastic CD30 positive cells in our case were found in biopsied skin, lymph node, and bone marrow, which implicated systemic disease. Primary ALCL with dissemination into lymph node was not acceptable, because of the primary involvement of lymph nodes, and then skin affection. The overlap is possible between ALCL and Hodgkin lymphoma (HL). Cutaneous involvement in HL is usually nonspecific; true tumoral infiltrates occur in only 1% of patients with systemic HL. Primary cutaneous Hodgkin lymphoma is even more rare (8). In HL Hodgkin cells are usually present, whereas Reed-Sternberg cells are detected in only about half of the cases. In addition, small lymphocytes, histiocytes, neutrophils, eosinophils, and plasma cells are admixed. Immunophenotyping reveals reactivity of Hodgkin and Reed-Sternberg cells for CD30. CD15 is frequently expressed but can be negative. CD45RO is not expressed (8).

Secondary ALCL may arise by transformation from another, usually CD30, lymphoma (most frequently cutaneous T-cell lymphomas). Transformed mycosis fungoides (MF) may be difficult to differentiate from ALCL and lymphomatoid papulosis, because all can be CD30⁺ and display anaplastic large cells. Distinguishing features may be the presence of small, intermediate, and large atypical lymphocytes in addition to the large anaplastic cells in transformed MF and pertinent clinical features such as spontaneous regression of disease in lymphomatoid papulosis or a history of extensive skin plaques in MF (9). Histopathology of MF reveals atypical cells with cerebriform, and sometimes hyperchromatic nuclei. Cells are mostly confined to the epidermis. The presence of intraepidermal collections of atypical cells, Pautrier microabscesses, is a highly characteristic feature, but is observed in only a minority of cases (10). This transformation is usually associated with a more aggressive behavior and shorter survival (11). Our patient never had skin changes prior this disease.

Distinction of ALK⁺ ALCLs and ALK⁻ ALCLs (which is only achievable by immunohistochemistry) is clinically important because the former usually affects younger patients and shows a more favorable clinical course. ALK⁺ ALCL appears to benefit from chemotherapy more than ALK⁻ (12).

Our patient had a good response to the first cycle of chemotherapy.

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