Chapter 12

CD30-Positive Anaplastic Large Cell Lymphoma Cell Lines

Hermann Herbst and Hans G. Drexler
Gerhard-Domagk Institute of Pathology, University of Münster, Domagkstr 17, 48129 Münster, Germany, and DSMZ-German Collection of Microorganisms & Cell Cultures, Department of Human and Animal Cell Cultures, Braunschweig, Germany. Tel: +49-251-835-6752; Fax: +49-251-835-5460; E-mail: herbsth@uni-muenster.de.

1. INTRODUCTION

In the late 1970s, the application of the monoclonal antibody Ki-1 (CD30) to anaplastic malignancies led to the recognition of a new entity of malignant lymphomas, CD30 (Ki-1 antigen)-positive anaplastic large cell lymphoma (“Ki-1 lymphoma”, ALCL) [52,53]. On the basis of conventional histology alone, ALCL had previously been diagnosed as Hodgkin’s sarcoma, malignant histiocytois, malignant fibrous histiocytoma, or even as non-hematopoietic malignancies such as undifferentiated sarcoma, undifferentiated carcinoma, or amelanotic melanoma. These lymphomas were recognized as a distinct entity of high grade B- and T-cell lymphomas in the updated Kiel classification of non-Hodgkin lymphomas (NHL) [51] and are included in the Revised European-American Lymphoma (REAL) classification as a type of high grade T-/null-cell lymphoma and as a variant of diffuse large cell lymphomas of B-cell type [23]. As there is some overlap with Hodgkin’s disease (HD), distinguishing ALCL with features of HD from lymphocyte depleted HD is a matter of ongoing debate.

2. CHARACTERISTICS OF ALC LYMPHOMAS

Clinically, ALCL presents most frequently in lymph nodes, often with subsequent infiltration of extranodal tissue. Among primary extranodal ALCL, cutaneous lesions are the most prevalent. ALCL may arise secondary to HD, lymphomatoid papulosis, mycosis fungoides, pleomorphic T-cell lymphoma
or T-cell lymphoma of angioimmunoblastic (AILD) type. The age distribution of primary ALCL revealed a bimodal pattern similar to HD, whereas ALCL arising simultaneously with or subsequent to other lymphomas showed a single peak in the fifth decade [52,53].

Histologically, the tumors are characterized by a preferential perifollicular involvement of lymph nodes by tumor cells often growing in coherent sheets with initial sparing of germinal centers, sinusoidal dissemination, and occasional foci of necrosis. The tumor cell morphology comprises a spectrum ranging from large pleomorphic cells with abundant, often basophilic, cytoplasm and irregularly shaped nuclei containing multiple small nucleoli or a single prominent, often rod-shaped nucleolus, to cells with more regular, rounded nuclei frequently containing a single nucleolus. The cells have a high mitotic rate and in many ALCL cases multinucleated tumor cells, often resembling Reed-Sternberg cells, may be found [52,53].

Unlike HD, where CD30 staining is a useful but not absolutely necessary diagnostic adjunct, the diagnosis of ALCL by definition requires the expression of the CD30 antigen in all of the tumor cells. Other activation antigens such as the low-affinity interleukin-2 receptor (CD25), class II histocompatibility antigens (HLA-DR), CD70 and proliferation-associated antigens such as the transferrin receptor (CD71) are usually found on ALCL tumor cells. Because activation antigens are not lineage specific markers, interest has centered on the study of cell type characteristic molecules. Similar to antigen- or mitogen-activated peripheral blood lymphocytes, which cease to express CD45 molecules, the three forms of the leukocyte common antigen (CD45, CD45RA, and CD45RO) are variably expressed on ALCL cells. Early lymphoid antigens present on precursor B- and T-cells, such as CD10 or terminal nucleotidyl transferase (TdT), or macrophage antigens, are usually not expressed by CD30+ malignancies. ALCL of T-cell type occurs more frequently than ALCL of B-cell type, and few cases do not express B- and T-lymphoid marker molecules if a sufficient panel of antibodies is applied. Primary cutaneous ALCL are generally of T-cell type [27]. T- and null-cell ALCL have a phenotype of cytotoxic cells with expression of granzyme B, T-cell-restricted intracellular antigen (TIA)-1 and granule membrane (GMP-17) proteins as well as perform transcripts [19]. The clinical relevance of these phenotypic details has been challenged by the finding of a generally better outcome in primary ALCL of either T- or B-cell type, i.e., independent of the immunophenotype, in adults as compared to other diffuse large cell lymphomas [56].

In contrast to HD, which appears to be a neoplasm of constitutively cytokine-secreting cells, a limited body of data is available on the expression of cytokines in ALCL. Although CD25 (IL-2 receptor)-positive, these lymphomas do not express IL-2 [43], thus excluding the possibility of an