T-cell lymphoma

471 B-CELL CLONALITY IN ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA

D. Stefanov[1], M. Sinitsyna[2], A. Kovrigina[2], I. Poddubnaya[1]
[1]Department of Oncology, Russian Medical Academy for Postgraduate Education, Moscow, Russian Federation, [2]Department of Pathology, N.N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation

Introduction: Angioimmunoblastic T-cell lymphoma (AITL) is one of the most common peripheral T-cell lymphoma subtypes in Western countries and in Russia, accounting for 25% to 30% of cases. It is characterized by primarily advanced disease with stage III and IV in more than 80% of cases, and dismal prognosis with a median survival < 3 years in most studies. One of the main pathologic features of AITL is the principal role of microenviroment consisting of non-neoplastic B-cells, T-cells and follicular dendritic cells, which typically represent a quantitatively major components of AITL. The expression and significance of B-cell component needs further investigation.

Materials and Methods: We have enrolled 27 patients with AITL, diagnosed or treated in N.N. Blokhin Cancer Research Center from 2007 till 2010. Median age was 60 years (range, 43–77). Advanced clinical stages (III and IV) were diagnosed in 78% of cases (n = 21). To evaluate B-cell component of tumor tissue we have performed polymerase chain reaction (PCR) from paraffine-embeded tissues, taken from tumor samples at diagnosis. The assessment of B-cell clonality was performed by evaluating immunoglobulin heavy chain (IgH) rearrangements in framework regions II (FR II) and III (FR III).

Results: The analysis was performed on 23 samples. Quality or quantity of tissue samples obtained from four patients was not enough to perform PCR. Monoclonal IgH rearrangements were detected in 7 patients (30,4%). In five cases both FR II and FR III reactions have revealed monoclonality, in two cases it was either FR II or FR III. In 6 cases (26,1%) one or both reactions have shown oligoclonal B-cell population (from two to nine peaks).

Conclusions: CHOP or CHOP-like chemotherapy is considered to be the standard treatment of AITL. This is largely due to the disease rarity, which made the researchers to establish therapeutic regiments in large trials with different lymphoma subgroups in them. Therefore AITL is still considered to be relatively chemoresistant to standard regiments with no specific therapeutic approaches established for it. Recently, however, new insights on biological features of this disease have provided us with new possible treatment options for patients with AITL. The detection of monoclonal B-cell population in one third of patients still needs further analysis to detect possible correlation between this biological feature and clinical behavior of the disease, and can be considered as a basis for evaluation of anti-CD20 antibodies efficacy in this disease.

472 B- AND T-CELL FEATURES OF ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA AS PATHOGENETIC BASIS FOR NEW CLINICAL APPROACH

M. Sinitsyna[1], D. Stefanov[2], E. Zakharova[3], D. Osmanov[4], A. Kovrigina[1], I. Poddubnaya[2]
[1]Department of Pathology, N.N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation, [2]Department of Oncology, Russian Medical Academy for Postgraduate Education, Moscow, Russian Federation, [3]Laboratory of Gene Therapy, Institute of Gene Biology, Moscow, Russian Federation, [4]Department of Oncology, N.N. Blokhin Russian Cancer Research Center, Moscow, Russian Federation

Introduction: AITL is now intensively reviewed in the light of new pathogenetic diagnostic criteria. According to the data of N.N. Blokhin Russian Cancer Research Center, including review of 99 biopsies with the diagnosis of nodal peripheral T-cell lymphoma (excluding ALCL), incidence of AITL is 56%, PTCL, NOS – 46%. Polymorphic composition of lymphoma, its poor clinical course have prompted detailed study of the various components of the tumor in terms of possible therapeutic modification

Patients and Methods: 55 biopsies with AITL diagnosed in N.N. Blokhin RCRC (2005-2010) were assayed using morphological, immunohistochemical (IHC) and PCR studies (TCR-gamma) on paraffin material. Ratio of men: women 1:1,1, median age 60 years. The IHC panel included CD3, CD4, CD10, CD20, CD23, CD30, EBV (LMP1), BCL-6, PD1 (NAT105), CXCL13, characterizing the presence of FDC proliferation, the origin of the tumor from follicular T-helper cells, and VEGF

Results: 4 morphological variants AITL were revealed: hyperplastic - 5 (9,1%), perifollicular- 1 (1,8%), interfollicular- 4 (7,3%), diffuse growth - 45 (81,8%). In all cases B-cell population including discrete large cells was presented in various degrees. Large B-cells were EBV-positive in 75%. The marker of follicular origin CD10 was detected in 77% of neoplastic cells, BCL-6 - 58%, PD1 (activated reactive T cells and tumor cells) - 100%, CXCL13 (neoplastic cells) in 100 %. Extrafollicular proliferation of FDC was insignificant in hyperplastic perifollicular variants and identified as intensive proliferating network in other morphologic variants. PCR has revealed monoclonal population of T-cell component in 14 biopsies, biclonal – in 6, oligoclonal – in 4, polyclonal – in 5 cases. Expression of VEGF in proliferating endothelial cells and neoplasticT cells was presented in 60% of observations

Conclusion: The unique polymorphism and biological peculiarities of different components in AITL determines its clinical features and prognosis. Taking into consideration the CD20+ EBV+ trigger pathogenetic model our data provide new perspective on the possible significance of the drugs with anti-angiogenic, anti-EBV virus, or anti-CD20- targets that should be studied in combinations with chemotherapeutic regimens for AITL in clinical trials.

473 ALK +/- ANAPLASTIC LARGE CELL LYMPHOMA (ALCL). "THE GREAT PRETENDER"

P. Ochoa [1], N. Tartas[1], M. C. Foncuberta[1], R. Burgos[1], A. Vitriu[1], R. Conti[1], H. Ferro[1], J. Korin[1], J. C. Sanchez Avalos [1]
[1]Hematology and Hematopoietic Transplant, Institute Alexander Fleming, Buenos Aires, Argentina

Introduction: ALK +/- ACLC is a non Hodgkin's lymphoma, generally of T cell origin, with better prognosis than other T-cell lymphomas, specially those which express the anaplastic large cell kinase (ALK). Although we have seen only ten patients in the last decade, the reason what prompt us to tell our experience, is its unusual clinical presentation that lead us to coin the name ''The great pretender'' for this type of lymphoma.

Material and Methods: We retrospective reviewed the clinical charts of the cases of ALCL diagnostic in our service during the last decade.

Results: Ten cases were classified as ACLC ALK +/-. Five male, median age 48.5 years (range: 22-65). The initial symptom was: fever 5/10, abdominal pain 3/10. Two patients had history of dermatological disease (lymphomatoid papulosis and PLEVA). 7/10 presented with extranodal disease at diagnosis: bone 3, lung 2, skin 1, small intestine 1. One patient relapses as menigeal lymphomatosis. The median time between the initial symptom and diagnosis 3 months (range: 1 – 10). In six patients the initial diagnosis resulted wrong: sarcoma, metastasis of indeterminate origin, hemophagocytic syndrome secondary to EBV, diverticular disease, SIHAD. In 8 cases the ALK inmunostaining was performed, in 5 resulted positive. In 5 cases the treatment was PROMACE – CYTABOM, in 3 DAEPOCH, CDE-P in 2. 9 achieved complete remission. 1 received autologous hematopoietic transplantation as consolidation of the CR1. 1 resulted refractory and is under salvage chemotherapy.3 relapsed within the year of the end of the treatment, received salvage chemotherapy and autologous hematopoietic transplantation, 2 are alive and the other died with progression. 9/10 is alive with a median of follow – up of 62 months (range: 16 – 112)

Conclusions: Almost 50% of our patients were initially wrongly diagnosed as having solid tumors or serious infections. Initial extranodal compromise of lung and bones contributed to the clinical confusion. Besides, the histological findings with sinusoid infiltration might have played a role. We think that it must be stressed that this curable type of lymphoma might be confused with other entities. With a high degree of clinical suspicion and a proper hematopathologic study, including CD30 and ALK inmunostaining, the diagnosis can be made and the great pretender can be unmasked.