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Leukaemia Section

Mini Review

Adult T-cell leukemia/lymphoma (ATLL)

Antonio Cuneo, Gianluigi Castoldi

Hematology Section, Department of Biomedical Sciences, University of Ferrara, Corso Giovecca 203, Ferrara, Italy (AC, GC)

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Clinics and pathology

Phenotype/cell stem origin

This is a T-cell lymphoid neoplasia caused by HTLV1 infection. The phenotype is CD3+, CD5+, CD7- with positivity for the CD4 and CD25 molecules in the majority of the cases.

Etiology

Pathogenesis of the disease: ATLL is associated with HTLV-1 infection of the tumour clone in 100% of the cases. The interval between HTLV-1 infection and the onset of lymphoma is long (10-40 years) and only <5% of infected people actually develops the disease. HTLV-1 produces a trans-regulatory protein (Tax) inducing interleukin-2 (IL-2) and IL-2 receptor expression and consequent polyclonal CD4 cell growth. This T-cell population is at risk for the development of genetic and cytogenetic changes leading to lymphoma.

Epidemiology

The disease affects adult people. Clusters were observed in Japan and in the Caribbean; sporadic cases were reported in Western countries.

Clinics

The disease usually runs an aggressive course, with peripheral blood and bone marrow involvement, diffuse adenopathies, hepatomegaly, bone lesions and hypercalcemia. Smouldering or chronic forms were also observed.

Pathology

The lymph node architecture is effaced by a diffuse proliferation of small and large lymphoid cells having pleomorphic cytological features. In the peripheral blood the neoplastic cells often display a lobated nucleus (flower cells); diffuse bone marrow infiltration is found in virtually all cases.

Treatment

Multiagent chemotherapy usually attains only partial, short lasting responses. Highly active anti viral therapy with zidouvidine and interferon-alpha may be beneficial in some cases.

Prognosis

Patients with aggressive disease usually survive less than 1 year; less than 10% of the patients survive more than 5 years. Longer survival (> 2 years) can be observed in rare patients presenting a chronic or a smouldering form.

Cytogenetics

Note

The karyotype almost invariably shows a high degree of complexity and variability. Aneuploidy and more than 6 chromosome breaks were observed in the majority of cases. The most frequent gains include trisomy 3, trisomy 8, trisomy 9 and trisomy 21; monosomies involve chromosome 4, 8, 10 and 22. Breakpoints clusters are found at 1p and 1q, at 3q, 6q, 7q, 10p, 12q, 13q, 14q, 17p and 21p. Multiple breaks and aberrations of some of these chromosome regions may predict for an inferior outcome.

Cytogenetics molecular

Comparative genomic hybridization (CGH) studies revealed that the most frequent regions of DNA gains are located at 14q, 7q and 3p; whereas frequent losses involve sequences at 6q and 13q. Gain of 14q32 may be a recurrent specific abnormality in ATLL. Aggressive forms display more genomic aberrations than chronic forms. The number of chromosomal

imbalances correlates with clinical outcome. Different hybridization patterns, suggesting clonal evolution, can be observed when analysing material from different sites or material taken at different time points in the same patient.

Upregulation of gene encoding for ribosomal proteins, proteosome subunits, translation factors was identified in acute vs chronic phases of the disease. Many of these genes are located in regions amplified by chromosome rearrangements. Downregulation of genes involved in immune response was also documented.

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