C2. PROGNOSTIC FACTORS ASSOCIATED TO THE BIOLOGY OF THE TUMOR PROCESS IN CLASSIC HODGKIN LYMPHOMA

Andrei Coliţă
Colţea Clinical Hopital, Bucharest

Classical Hodgkin's lymphoma (CHL) represents 11% of all lymphomas but, with the highest incidence among young adults with ages from 20 to 34 years. Using current treatment strategies, over 70% patients can be cured. Still, 15-20% patients in early stages (Stage I, II), as well as 35-40% of those in advanced stages (III and IV) present relapses or resistance to first line therapy.

Progress made in the past 15 years allowed a better understanding of the biology of CHL and prognostic implications regarding disease evolution and therapeutic response.

Hodgkin's Lymphoma represents a peculiar type of cancer by the fact that malignant cells (Reed-Sternberg cells - RSC) represent only 2% of the tumour mass, the rest being represented by a rich inflammatory infiltrate consisting of a great variety of non-malignant cells (B and T lymphocytes, plasma cells, eosinophils, histocytes, fibroblasts, granulocytes) which form a RSC-driven micro-environment that ensures tumour cell survival.

RSC derive from B lymphocytes of the lymphatic germinal centre which have suffered a clonal rearrangement of genes coding for immunoglobulin heavy chains (Ig) and which are deficient in Ig surface expression and the expression of genes involved in differentiation. Despite these phenomena, RSC does not undergo apoptosis due to the disturbance of several signalling pathways as a consequence of mutations, fusions and altered expression of genes involved in these mechanisms. Changes in the expression of these genes may influence disease progression and therapeutic response.

RSC synthesizes and releases a variety of cytokines and chemokines which are responsible for recruiting the cells forming the tumour micro-environment.

The prognostic importance of cell composition in the non-malignant infiltrate around RSC has been observed ever since the description of histological subtypes. Gene expression and phenotypic changes in the cells that form the tumor microenvironment may influence the disease outcome.

Several studies have shown, as well, the predictive value of the serum levels of chemokine and cytokine molecules and their soluble receptors' presence in serum.

Research in biological characteristics of both RSC and cells and soluble factors of the tumour micro-environment represent the latest line of research in this pathology, in the attempt to describe biomarkers with a prognostic role.