2. Hairy cell leukemia: New understanding of biology and treatment

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Introduction

Historical perspectives

The term Leukemic reticuloendotheliosis, later to be known as hairy cell leukemia (HCL), was first applied by Ewald [1] to a patient with a fulminating, fatal disorder characterized by the circulation of large numbers of abnormal cells in the blood. Although his publication is sometimes cited as the first description of HCL [2], in retrospect it seems more likely that he was actually observing a patient with a form of acute myelogenous leukemia.

In describing the circulating cells, Ewald wrote:

The cells vary greatly in size ranging from twice to eight times the diameter of the red cell. The cytoplasm is large, mostly oval or polygonal, weakly basophilic in many cells with a trace of redness. A light paranuclear zone is sometimes pronounced. The nucleus is relatively large, rarely round, usually polygonal or folded; often two nuclei are present in a cell. The nucleus shows an indistinct structure that resembles that of lymphocyte nuclei but is not as homogeneous as the nucleus of the usual stem cell. Usually the number of distinct nucleoli varies from 1 to 5. None of the cells were devoid of nucleoli. All of the cells had distinct azure granulations which were sometimes so pronounced that the entire cell appeared dark and one could hardly recognize a boundary between the nucleus and cytoplasm. In summary we would state: The cells, which represented approximately 95% of the leukocytes, are most similar to the usual stem cells; but they also show striking differences which speaks for their being a special type of cell.

Drawings of the abnormal cells (figure 2-1) tend to reinforce the idea that this was not a case of HCL.

The existence of leukemic reticuloendotheliosis gained more general recognition when in 1958 Bouroncle et al. described 26 patients with the
Das weiße Blutbild wird beherrscht von pathologischen Zellen, die keiner Form der gewöhnlichen Blutzellen oder deren Jugendformen, die bei der leukämischen Myelose auftreten, gleichen.


Figure 2-1. Leukemic reticuloendotheliosis (Ewald 1923).

disorder [2]. Many other terms have been used to describe this type of leukemia, including histoleukemia, medullosplenic-histiolymphoctyosis of primitive appearance, reticulum cell leukemia, and lymphoid myelofibrosis [3]. These unwieldy and inaccurate names were gradually superseded by the more graphic hairy cell leukemia after Schrek and Donnelly referred to the neoplastic cells as ‘hairy cells’ in 1966 [4].

Natural history

The natural course of the disease is extremely variable. The disease is chronic and, at diagnosis, the patients are often symptomatic, manifesting hematologic abnormalities. In a series of 102 patients, at presentation 86 had anemia, 84 thrombocytopenia, and 78 neutropenia [3]. Splenomegaly was present in 93 patients. Bleeding and infectious complications occur with increasing frequency as the disease progresses, yet not all patients with HCL require therapy. In 10% of patients, usually elderly males with moderate splenomegaly, progression is extremely slow; these patients never require therapeutic intervention [5]. The median survival was previously reported as five years [3,5]. Although efforts were made to relate survival to the specific therapy administered, it is difficult to draw conclusions from such an analysis, since treatment was notoriously ineffective until the 1980s. Also, the patients subjected to treatment were often those whose disease was pursuing a more aggressive course.